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WASHINGTON D.C., 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

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MEMORANDUM

Subject: Myclobutanil Problem Formulation for Registration Review

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The Environmental Fate and Effects Division (EFED) has completed the preliminary problem formulation (attached) for the ecological risk and drinking water exposure assessments to be conducted as part of the Registration Review of the fungicide myclobutanil (PC Code 128857). This document is intended to provide an overview of what is currently known regarding the environmental fate and ecological effects associated with myclobutanil and its degradation products, and outlines uncertainties regarding attributes of the parent compound and its transformation products. It describes the preliminary ecological risk hypothesis and the processes that will be used during the completion of the preliminary ecological risk assessment in support of Registration Review.

As noted in Section 5, additional data will be needed for the toxicological properties of myclobutanil to complete the risk assessment and registration review process. Additional studies EFED recommends be requested include avian acute oral and honey bee toxicity studies, estuarine/marine invertebrate studies, freshwater fish studies, aquatic (vascular and non-vascular) plant and terrestrial plant studies.

Additional fate and transport studies are not being requested for myclobutanil because a reasonably conservative risk assessment can be conducted with existing data gaps; however, additional fate data could assist in refining the assessment.

Many of the myclobutanil product labels do not specify the maximum number of applications that can be applied per year or crop cycle and/or the number of crop cycles per year. Some labels are missing a single maximum application rate. We request that in completing the Use Summary Table, the registrants provide this information.

INTRODUCTION

Myclobutanil is a systemic fungicide used to control powdery mildew on a number of crops. It is a triazole fungicide in the conazole class of fungicides. Myclobutanil is classified as a sterol biosynthesis inhibitor (SBI) and is further classified as a demethylation inhibitor (DMI) fungicide because it inhibits the enzyme sterol 14-demethylase, which disrupts the ergosterol biosynthesis pathway that is vital to fungal cell wall structure and function (FRAC 2012, Roberts and Hutson 1999). Myclobutanil is a Group 3 Fungicide.

Myclobutanil was first registered in the United States in 1984. Based on the Summary Level Usage Analysis (SLUA) report, between 2004 -2012, the agricultural use with the highest usage (in pounds a.i. applied per year) is grapes with 50,000 average pounds used. The next highest usage crops were apples (20,000 average pounds per year) then almonds, tomatoes, and cherries with 8,000, 7,000, and 5,000 pounds used per year, respectively. Usage data are currently not available for the non-agricultural uses of myclobutanil.

All current labeled uses of myclobutanil include the following food uses: almond, apple, apricot, artichoke, asparagus, beans (succulent), blackberry, boysenberry, caneberries, canistel, carrot (including tops), cherry, chrysanthemum garland, cotton, cucurbits (pumpkin, squash, watermelon), currant, eggplant, gooseberry, grapes, hops, lettuce (head, leaf), loganberry, mamey (mammee apple), mango, mayhaw (Hawthorn), mint/peppermint/spearmint, nectarines, okra, olallie berries, papaya, peach, pepper, pimento, plum, prune, raspberry (black, red), sapodilla, sapote white, soybeans (unspecified), star apple, strawberry, subtropical/tropical fruit and tomato. Non-food/non-feed uses include bluegrass, commercial/industrial lawns, cotton (seed), Douglas Fir (seed orchard, shelter belt), golf course turf, grasses grown for seed, household/domestic dwellings (outdoor premises), hybrid cottonwood/poplar plantations, loblolly pine (forest), ornamental and shade trees, ornamentals (herbaceous plants, lawns and turf, sod farm (turf), unspecified, woody shrubs and vines), residential lawns and slash pine forest (USEPA 2014 a.).

Application types include broadcast (aerial and ground), chemigation, directed spray, foliar treatment, ground spray, high volume spray (dilute), low volume spray (concentrate), seed treatment, spot treatment, and spray (USEPA 2014 a.).

Based on current labels, the maximum single application rate ranges from 0.1037 to 1.4 pounds of active ingredient per acre (lb a.i./acre) and up to 16 applications per year for some uses. The highest annual application rates generally are found in the ornamentals (sod farms, lawns and turf) and residential lawns. However, the number of applications of myclobutanil that can be applied per calendar year or the maximum annual application rate for a given use is not explicitly stated on many of the current labels.

The chemical profile produced by BEAD, located in the docket, lists the use patterns of maximum exposures for the current uses of Myclobutanil. EFED will use application scenarios that result in maximum exposure scenarios for a given use for the risk assessment. Any absence of information on the labels that specifies the maximum single application rate, the application interval, the annual maximum rate allowed (lb a.i./year), or application method may result in conservative assumptions.

Previous Ecological Assessments

Myclobutanil has been assessed a number of times for new uses including Section 18 assessments since the original registration in 1984. Such assessments include a 2009 California Red-Legged Frog Endangered Species Assessment and Section 3 Ecological Risk Assessment for Myclobutanil (October 12, 2007) (DP336613). EFED evaluated these assessments and others for myclobutanil in association with the current toxicity, exposure, and use information to determine if sufficient data are available and if further updates are needed to support registration review. In some of the previous assessments, risks were assessed using the parent compound only, whereas others took into consideration degradates of concern using the total toxic residue (TTR) approach. In the most recent assessment conducted in 2012, stressors of concern for aquatic organisms were considered to be myclobutanil and 1,2,4-triazole, while stressors of concern for terrestrial organisms were considered to be myclobutanil, the plant metabolite RH-9090, 1,2,4-triazole, and triazole conjugates 1,2,4-triazole alanine and 1,2,4 triazole acetic acid (also referred to as triazole alanine and triazole acetic acid) (D402503). Based on the review of available toxicity data and the ECOSAR results considered in the development of this Problem Formulation, the aquatic risk assessment conducted for registration review will likely consider only the parent compound, while the approach to terrestrial risk will remain the same.

Based on the various past assessments which spanned a range of application rates and patterns, risk tended to be greatest for freshwater fish (acute), marine/estuarine invertebrates (acute), birds (acute and chronic), and mammals (acute and chronic) depending on the use patterns and application rates. At the time of many of these assessments, certain toxicity data were not available [e.g. terrestrial plants, aquatic vascular plants, chronic avian, chronic invertebrates (freshwater and marine/estuarine) or acute marine/estuarine fish, terrestrial invertebrates] so risk was not assessed quantitatively or was presumed in the absence of data. A qualitative summary of previous risk concerns identified is provided in Table 2.

Table 2. Summary of Previous Risk Concerns Identified for Myclobutanil[a]

Exposure Basis	Birds	Mammals	Terrestrial Plants	Terr. Inverts. (honey bee hazard)	Fish	Aquatic Inverts	Aquatic Plants	Ground Water	Persistence	Degradates of Concern
Acute	**Yes**	**Yes**	**Yes[b]**	**No**	**No**	**Yes[c]**	**Yes[b]**	**No**	**Yes**	**Yes**
Chronic	**Yes**	**Yes**			**No**	**No**				

a. At least one LOC has been exceeded in previous assessments
b. Based on lack of toxicity data, risks were assumed
c. Estuarine/marine invertebrates only

Previous Drinking Water Assessments

The most recent drinking water assessment (DWA) for myclobutanil was conducted in 2012, which re-assessed the use with the highest application rate, turf (USEPA, 2012 a.). The surface water estimated drinking water concentrations (EDWCs) for myclobutanil were calculated using a Tier II model (PRZM-EXAMS) and took into account additional aerobic aquatic metabolism data and revised percent crop area guidance (USEPA, 2012 b.). The estimated groundwater concentrations of myclobutanil were calculated using PRZM-GW. The groundwater EDWCs were lower than the surface water EDWCs, and EFED recommended using the surface water EDWCs for human health (dietary) risk assessment. The maximum concentrations of myclobutanil in surface water were estimated to be 218 µg/L for the 1-in-10-year annual peak, 172 µg/L for the 1-in-10-year annual average, and 117 µg/L for the 30 year annual average. The maximum peak concentration of myclobutanil in groundwater was estimated to be 41.5 µg/L.

The most recent EDWCs for 1,2,4-triazole, 1,2,4-triazole alanine, and 1,2,4-triazole acetic acid were calculated in support of the 2006 aggregate assessment for triazole-derivative fungicides (USEPA, 2006 a.; USEPA, 2006 b.). The highest 1,2,4-triazole, 1,2,4-triazole alanine, and 1,2,4-triazole acetic acid EDWCs calculated in this assessment were for the myclobutanil turf use, which resulted in the surface water EDWCs (using PRZM-EXAMS) shown in **Table 3.** A groundwater EDWC of 1.06 µg/L was calculated for 1,2,4-triazole using SCI-GROW. More details on the methods and assumptions used to calculate these EDWCs may be found in the aggregate assessment.

Table 3. Surface Water EDWCs for 1,2,4-Triazole and its Conjugates of Concern from Use of Myclobutanil on Turf[a] (D320682)

Myclobutanil Degradate	Estimated Surface Water Drinking Water Concentrations (µg/L)		
	1-in-10-year annual peak	1-in-10-year annual mean	36-year annual mean
1,2,4-Triazole[a]	41.0	11.0	2.69
1,2,4-Triazole Acetic Acid (TAA)[b]	75.4	20.2	4.95
1,2,4-Triazole Alanine (TA)[c]	92.7	24.9	6.08

[a] Golf Course Turf PA golf course turf scenario; application rate based upon 6 applications of myclobutanil at 1.73 lb a.i./A; 10.38 lb a.i./A/yr. 1,2,4-Triazole application was obtained from molecular weight conversion times myclobutanil application rate times max percent formation rate for triadimefon (turf = (69.0/288.78)*1.73*0.307), as this was believed to be the maximum percent formation rate for all fungicides in the conazole class.
[b] TAA = (127.10/69.0)*1,2,4-Triazole concentration.
[c] TA = (156.15/69.0)*1,2,4-Triazole concentration.

Clean Water Act Programs

Myclobutanil is not identified as a cause of impairment for any water bodies listed as impaired under section 303(d) of the Clean Water Act. Total Maximum Daily Load (TMDL) criteria have not been developed for myclobutanil (http://iaspub.epa.gov/tmdl_waters10/attains_impaired_waters.tmdls?p_pollutant_group_id=885). Aquatic benchmarks have been established for myclobutanil for freshwater fish (acute 1,200 µg/L, chronic 980 µg/L), freshwater invertebrates (acute 5,500 µg/L), and freshwater nonvascular plants (acute 830 µg/L) (http://www.epa.gov/oppefed1/ecorisk_ders/aquatic_life_benchmark.htm). Any data submitted or otherwise located as part of the registration review process may be used to revise or establish new aquatic life benchmarks, if applicable.

1. ENVIRONMENTAL FATE AND TRANSPORT

Physical and Chemical Properties of Myclobutanil

Selected physicochemical properties of myclobutanil are shown in **Table 4**. Based on these properties alone, volatility is not expected to be a major dissipation pathway for myclobutanil, and myclobutanil is not expected to bioaccumulate.

Table 4. Selected Physical/Chemical Parameters of Myclobutanil

Chemical name	Property	Data Source (MRID)
Molecular weight	288.775 g/mol	-
Aqueous Solubility	142 mg/L at 25°C	00141683 48951203
	Milli-RO Water: 118 mg/L at 20°C pH 4.0 buffer: 115 mg/L at 20°C pH 7.0 buffer: 107 mg/L at 20°C pH 9.0 buffer: 115 mg/L at 20°C	46802501
Vapor Pressure	1.60×10^{-6} torr at 25°C	48951203
	$< 9.75 \times 10^{-6}$ torr at 25°C	46802501
Henry's Law Constant	3.25×10^{-09} atm m^3/mole at 25°C	Calculated
Octanol-water partition coefficient (log Kow)	2.47 at 22°C	00162541
	2.84-2.98 at unspecified ambient temperature Mean: 2.94	00141683

Environmental Fate and Transport of Myclobutanil

Table 5 summarizes the environmental fate properties of myclobutanil, while **Appendix A** provides the chemical structure of myclobutanil and its major degradation product, 1,2,4-triazole. Due to its persistence and mobility, myclobutanil applications may lead to surface water contamination through spray drift, runoff, sediment erosion and groundwater contamination through leaching. Myclobutanil has been detected in rain in several agricultural watersheds in California (Vogel et al. 2008); thus, there is also a potential for atmospheric transport.

Myclobutanil degrades rapidly as a result of aqueous photolysis (4 day half-life) and is relatively stable to soil photolysis (144 day half-life). Myclobutanil is stable to hydrolysis. The only aerobic soil metabolism study available for myclobutanil indicates that the pesticide undergoes non-linear microbial degradation in aerobic soil, with a Double First-Order in Parallel (DFOP) half-life of 750 days. Myclobutanil appears to slowly degrade in a linear fashion in aerobic aquatic environments (half-lives of 416 and 834) and is very persistent anaerobic aquatic environments. The wide range of half-lives in terrestrial field studies indicates that myclobutanil may dissipate rapidly or slowly depending on the environmental conditions.

Myclobutanil has the potential to leach into groundwater, as it is classified as moderately mobile (K_{foc} = 226 – 923) (FAO 2000). A leaching study conducted on one soil suggests that myclobutanil residues will remain primarily in the top 10 cm of soil, although residues were found at the 20 inch (maximum) depth and in leachate (MRID 00141681). The adsorption/desorption study results indicate that soil sorption of myclobutanil is highly influenced by soil acidity and soil cation exchange capacity. A regression analysis indicated that lower soil acidity results in increased soil sorption of myclobutanil; an increase in the pH by 1 increases the K_f by 3 (r-squared = 0.81; p-value < 0.05). Similarly, an increase of soil cation exchange capacity of 1 meq/100g results in an increase in the K_f of 0.7 (r-squared = 0.81; p-value < 0.05). Sorption may also be influenced by soil organic carbon content. The coefficient of variance is lower for the K_{foc}'s than for the K_f's, indicating a correlation between myclobutanil soil sorption and soil organic carbon content; however, a regression analysis of percent organic carbon versus K_f for the five soils did not find this relationship to be statistically significant.

Table 5. Chemical Properties and Environmental Fate Parameters of Myclobutanil

Parameter	Value*	Description	Source (MRID)	Study Status
Persistence				
Hydrolysis half-life	Stable	pH 5, 7, 9 at 22 ± 2.3°C	00141679	Acceptable
Aqueous photolysis half-life	4 days (IORE)	Study conducted at 31°C	00164560 40641501 40319801 40528801	Studies acceptable only in combination, not individually

Parameter	Value*	Description	Source (MRID)	Study Status
Soil photolysis half-life	144 days (SFO)	Lawrenceville silt loam pH 5.3 at 34°C	00164987 00164988	Studies acceptable only in combination, not individually
Aerobic soil metabolism half-life	750 days (DFOP)	Lawrenceville silt loam pH 5.3	00141680 00164561	Individual study acceptable
Anaerobic soil metabolism half-life	Stable	Lawrenceville silt loam flooded after 30 days under aerobic conditions Flood water not characterized	00141680 00164561	Individual study acceptable
Aerobic aquatic metabolism half-life (total system)	Rhine River 416 days (SFO) Pond 834 days (SFO)	Rhine River pH 7.36-8.53 at 17.1°C Pond pH 7.46-8.40 at 12.8°C	47454401	Acceptable
Mobility				
Adsorption– K_f	4.47 $^1/_n$ = 0.89	Hagerstown Clay Loam: 1.98% OC, soil pH 6.4, CEC 9.4 meq/100g	00141682	Supplemental
	1.46 $^1/_n$ = 0.89	Lakeland Agricultural Sand: 0.55% OC, soil pH 5, CEC 1.7 meq/100g		
	7.10 $^1/_n$ = 0.88	Lawrenceville Silty Loam: 1.19% OC, soil pH 6.1, CEC 11.9 meq/100g		
	9.81 $^1/_n$ = 0.85	Pasquotank Sandy Loam: 1.68% OC, soil pH 7.2, CEC 12.5 meq/100g		
	2.40 $^1/_n$ = 0.91	Cecil Clay: 0.26% OC, soil pH 4.7, CEC 6.9 meq/100g		
	5.05	**MEAN** Study conducted at "ambient" temperature		
Adsorption– K_{foc}	226	Hagerstown Clay Loam: 1.98% OC, soil pH 6.4, CEC 9.4 meq/100g		
	266	Lakeland Agricultural Sand: 0.55% OC, soil pH 5, CEC 1.7 meq/100g		

Parameter	Value*	Description	Source (MRID)	Study Status
	596	Lawrenceville Silty Loam: 1.19% OC, soil pH 6.1, CEC 11.9 meq/100g		
	584	Pasquotank Sandy Loam: 1.68% OC, soil pH 7.2, CEC 12.5 meq/100g		
	923	Cecil Clay: 0.26% OC, soil pH 4.7, CEC 6.9 meq/100g		
	519.04	**MEAN** Study conducted at "ambient" temperature		
Field Dissipation				
Terrestrial Field Dissipation Half-Life	9.36 days (IORE)	Winter wheat - Newtown, Pennsylvania Silty Loam, 0-3" depth (leached to deepest sampling depth of 6-12")	00164563 00164987	Acceptable
	80.7 days (SFO)	Winter wheat - Cleveland, Mississippi Loam, 0-3" depth (leached to deepest sampling depth of 6-12")		
	409 days (SFO)	Bare ground - Fresno County, California Sandy Loam (leached to deepest sampling depth of 18-24")	42181101	Acceptable
	243 days (IORE)	Bare ground - Santa Clara County, California Loam (leached to deepest sampling depth of 18-24")		
	81.6 days** (DFOP)	Turf – Baptistown, New Jersey Silt Loam (leached to deepest sampling depth of 18-24")	43087904	Supplemental

*All values have been re-estimated by the authors of this document. Representative half-lives are estimated SFO half-lives (for EFED modeling inputs) from a degradation curve that does not necessarily follow the SFO equation. Representative half-life values were calculated using nonlinear regression and SFO, DFOP, or IORE equations. The equations can be found in the document, Standard Operating Procedure for Using the NAFTA Guidance to Calculate Representative Half-life Values and Characterizing Pesticide Degradation (US EPA 2012). Representative half-life values calculated in this table do not include unextracted residues.

**Representative half-life calculated from post-treatment day 10 to the end of the study, as maximum myclobutanil concentrations were observed on day 10.

Transformation Products

Myclobutanil degrades to 1,2,4-triazole when subjected to light in aquatic environments or exposed to microbes in aerobic soil. In the aqueous photolysis study, 1,2,4-triazole comprised 49% of the applied radioactivity on day 30 of the study. In the aerobic soil metabolism study, 1,2,4-triazole comprised 18% of the applied radioactivity on days 150 and 180 of the study, declining to 13% at the end of the study (day 367). 1,2,4-triazole was observed at all depths in the terrestrial field dissipation studies and its formation ranged from 2.1% (6-12" segment) to 58.6% (3-6" segment). 1,2,4-triazole is the only major transformation product of myclobutanil observed in field and laboratory studies; however, the analytical methods used in those studies are rarely able to identify 1,2,4-triazole conjugate residues separately from 1,2,4-triazole. **Appendix A** provides additional detail on degradation of myclobutanil to 1,2,4-triazole in the environment, including degradate and conjugate structures.

Based on registrant-submitted laboratory and field studies, 1,2,4-triazole is persistent (average aerobic half-life = 645 days) and very mobile (K_f's 0.23 – 0.84) in the soil. 1,2,4-triazole's major routes of dissipation are leaching into groundwater and runoff into surface water.

Hydrolysis, aqueous photolysis, and soil metabolism are not major routes of 1,2,4-triazole degradation (hydrolysis half-lives 99 - 421 days; stable to aqueous photolysis). Microbial degradation of 1,2,4-triazole in aerobic soils is highly varied (half-lives from 20 days to stable) and consistently non-linear. The high variability in the half-lives may be explained, in part, by the application rate used in the aerobic soil metabolism studies; higher levels of application (1 to 50 ppm in soil) seem to suppress microbial degradation. On average, even with this variability, 1,2,4-triazole is persistent in aerobic soil. The average aerobic soil metabolism half-life for treatment levels at or less than 1 ppm is 197 days, while the average half-life incorporating treatment levels up to 50 ppm is 645 days. 1,2,4-triazole is moderately persistent in anaerobic soil (half-life 81 days).

1,2,4-triazole's major transformation products are the conjugate 1,2,4-triazole acetic acid and hydroxytriazole. Both transformation products are formed through microbial degradation in aerobic soils. In one aerobic soil metabolism study 1,2,4-triazole acetic acid comprised a maximum of 18% of the applied radioactivity (day 98), declining to 11.7% by the end of the study (day 293). In a separate aerobic soil metabolism study, hydroxytriazole comprised a maximum of 30.8% of the applied radioactivity (day 12), declining to 0.6% at the end of the study (day 180). 1,2,4-triazole acetic acid is also formed through anaerobic soil metabolism, and was observed at 50% of applied radioactivity on the last sample day of the only anaerobic soil metabolism study available for 1,2,4-triazole. 1,2,4-triazole alanine was also detected as a minor transformation product in the anaerobic soil metabolism study.

1,2,4-triazole has the potential to leach into groundwater, as it is classified as mobile to moderately mobile (K_{foc} = 48 - 202) (FAO 2000). Leaching studies conducted for 1,2,4-triazole suggest that the compound and its transformation products are mobile in a variety of soil types, with radiolabelled residues leaching to the maximum soil depth considered, 30 centimeters (MRIDs 00133372 and 45284030).

Field dissipation studies indicate that 1,2,4-triazole has the propensity to leach, as the compound was detected up to 12 inches soil depth in field plots. Adsorption/desorption study results indicate that soil organic carbon content and CEC do not influence soil sorption of 1,2,4-triazole. Although there is a statistically significant positive relationship between K_f and soil pH, an increase in soil pH of 1 only increases the K_f by 0.15 (r-squared = 0.76, p-value $\leq$ 0.05).

Table 6 summarizes the environmental fate properties of 1,2,4-triazole and 1,2,4-triazole acetic acid, while **Appendix A** provides additional detail on formation of 1,2,4-triazole transformation products in the environment, including degradate and conjugate structures.

Table 6. Chemical Properties and Environmental Fate Parameters of 1,2,4-Triazole and Conjugates

Parameter	Value*	Description	Source (MRID)	Study Status
1,2,4-Triazole				
Persistence				
Hydrolysis half-life	303 days (DFOP)	pH 5 acetate buffer at 25°C	00133373	Supplemental
	421 days (DFOP)	pH 7 phosphate buffer at 25°C		
	98.7 days (SFO)	pH 9 borate buffer at 25°C		
Aqueous photolysis half-life	Stable	pH 7 distilled water temperature not reported	45284026	Supplemental
Aerobic soil metabolism half-life	378 days (DFOP)	Les Barges (Swiss) silty loam 1 ppm applied pH 7.6 at 25°C	45284027	Supplemental
	70.1 days (IORE)	Laacher Hof AXXa (German) sandy loam ~0.06 ppm applied pH 6.9 (H_2O) at 20±2°C	45284032	Supplemental
	319 days (DFOP)	BBA 2.2 (German) loamy sand ~0.06 ppm applied pH 6.19 (H_2O) at 20±2°C		
	20.3 (IORE)	Laacher Hof A III (German) silt loam ~0.06 ppm applied pH 7.88 (H_2O) at 20±2°C		
	Stable (DFOP half-life 1,530 days)	Standard Soil 2.2 50 ppm applied pH 6.0 at 22±2°C	45297203	Supplemental
	Stable (DFOP half-life 1,550 days)	Standard Soil 2.3 50 ppm applied pH 5.5 at 22±2°C		
Anaerobic soil metabolism half-life	81.2 days (SFO)	Les Barges (Swiss) silt loam pH 7.31 at 20±2°C	45930701	Acceptable
Mobility				
Adsorption – K_f	0.84 $^1/_n$ = 0.90	Alpaugh Silty Clay: 0.65% OC, soil pH 8.8, CEC 30.5 meq/100g	40891501	Acceptable
	0.27 $^1/_n$ = 0.63	Hollister Clay Loam: 1.74% OC, soil pH 6.9, CEC 16.9 meq/100g		
	0.23 $^1/_n$ = 0.89	Lakeland Sand: 0.12% OC, soil pH 4.8, CEC 1.2 meq/100g		

Parameter	Value*	Description	Source (MRID)	Study Status
1,2,4-Triazole				
	0.73 $^1/_n$ = 0.92	Lawrenceville Silty Clay Loam: 0.70% OC, soil pH 7, CEC 6.6 meq/100g		
	0.72 $^1/_n$ = 1.02	Pachappa Sandy Loam: 0.81% OC, soil pH 6.9, CEC 11.1 meq/100g		
	0.56	**MEAN** Study conducted at 25±1°C		
Adsorption – K_{foc}	129	Alpaugh Silty Clay: 0.65% OC, soil pH 8.8, CEC 30.5 meq/100g		
	48	Hollister Clay Loam: 1.74% OC, soil pH 6.9, CEC 16.9 meq/100g		
	202	Lakeland Sand: 0.12% OC, soil pH 4.8, CEC 1.2 meq/100g		
	104	Lawrenceville Silty Clay Loam: 0.70% OC, soil pH 7, CEC 6.6 meq/100g		
	89	Pachappa Sandy Loam: 0.81% OC, soil pH 6.9, CEC 11.1 meq/100g		
	114	**MEAN** Study conducted at 25±1°C		
Field Dissipation				
Terrestrial Field Dissipation Half-Life	445 days (IORE)	Newtown, Pennsylvania Silty Loam, 0-3" depth (leached to 6-12" segment; study sampled to 36" depth)	45284025	Supplemental
	391 days (SFO)	Newtown, Pennsylvania Silty Loam, 0-3" depth (leached to deepest sampling depth of 6-12")	00164564	Supplemental
	525 days (SFO)	Cleveland, Mississippi Loam, 0-3" depth (leached to deepest sampling depth of 6-12")		
1,2,4-Triazole Acetic Acid				
Persistence				
Aerobic soil metabolism half-life	5.01 days** (IORE)	SP-2.1 (German) sand pH 5.2 at 20°C	46017601	Pending Review
	6.27 days** (IORE)	SP-2.2 (German) loamy sand pH 5.6 at 20°C		
	7.04 days** (DFOP)	SP-2.3 (German) sandy loam pH 6.3 at 20°C		

*All values have been re-estimated by the authors of this document. Representative half-lives are estimated SFO half-lives (for EFED modeling inputs) from a degradation curve that does not necessarily follow the SFO equation. Representative half-life values were calculated using nonlinear regression and SFO, DFOP, or IORE equations. The equations can be found in the document, Standard Operating Procedure for Using the NAFTA Guidance to Calculate Representative Half-life Values and Characterizing

Pesticide Degradation (US EPA 2012). Representative half-life values calculated in this table do not include unextracted residues.
**This aerobic soil metabolism study did not identify any conjugates or degradates of 1,2,4-Triazole Acetic Acid, even though transformation products formed to upwards of 75% applied radioactivity. It is possible that 1,2,4-Triazole Acetic Acid in combination with its conjugates of concern are persistent in aerobic soil, even though, based on the data in this study, 1,2,4-Triazole Acetic Acid is not persistent in aerobic soil.

2. RECEPTORS

Tables 7 and 8 provide a summary of the aquatic and terrestrial toxicity data, respectively, and the most sensitive surrogate species tested to characterize the potential acute and chronic ecological effects of myclobutanil. **Table 9** provides information on the most sensitive toxicity data available for myclobutanil degradates. All available toxicity data for myclobutanil degradates listed in **Appendix D**.

Table 7. Summary of the Most Sensitive Endpoints from Aquatic Toxicity Studies for Myclobutanil

Taxonomic Group	Study type	Surrogate Species	Toxicity	MRID (classification)	Acute Toxicity Classification
Freshwater fish	Acute	Bluegill Sunfish (*Lepomis macrochirus*)	96-hr **LC_{50}: 2.4 mg a.i./L** NOAEC = 1.5 mg a.i./L LOAEC = 2.7 mg a.i./L based on quiescence, loss of equilibrium and death.	00144285 (Acceptable)	Moderately toxic
	Chronic	Fathead minnow (*Pimephales promelas*)	NOAEC= **0.98 mg a.i./L**[1] LOAEC = 2.2 mg a.i./L based on a 9.7% reduction in body length. Total mortality at 8.5 mg a.i./L	00164986/ 40409201/ 40480401 (Acceptable)	N/A
Estuarine/ marine fish	Acute	Sheepshead minnow (*Cyprinodon variegatus*)	96-hr **LC_{50}: 4.7 mg a.i./L** NOAEC = 1.2 mg a.i./L LOAEC = 1.8 mg a.i./L (erratic behavior, darkened pigmentation, lethargy; fish at higher concentration levels also exhibited partial loss of equilibrium and rapid respiration). Mortality was 5% at 3.8 mg a.i./L and 100% at 6.3 mg a.i./L	42747903 (Acceptable)	Moderately toxic
	Chronic	N/A	No Data	---	---
Freshwater invertebrates	Acute	Water flea (*Daphnia magna*)	48-hr **EC_{50}: 11 mg a.i./L** NOAEC = 3.2 mg a.i./L LOAEC = 5.6 mg a.i./L (settled to the bottom). Mortality was 45% at 10 mg a.i./L and 90% at 18 mg a.i./L	00141678 (Acceptable)	Slightly toxic
	Chronic	Water flea (*Daphnia magna*)	**Estimated NOAEC using ACR= 3.9 mg a.i./L**[2]	No Study	N/A

Taxonomic Group	Study type	Surrogate Species	Toxicity	MRID (classification)	Acute Toxicity Classification
Estuarine /marine invertebrates	Acute	Eastern oyster (*Crassostrea virginica)*	96-hr **EC_{50}: 0.68 mg a.i./L** NOAEC = 0.48 mg a.i./L LOAEC = 0.78 mg a.i./L (shell deposition). Inadequate shell growth in controls may underestimate pesticide related shell growth effects. (Discussed in Section 4. Preliminary Identification of Data Gaps)	42747901 (Supplemental)	Highly toxic
		Mysid shrimp (*Americamysis bahia*)	96-hr **LC_{50}: 0.24 mg a.i./L** NOAEC could not be determined as effects seen at all dose levels (erratic swimming behavior, darkened pigmentation, lethargy). Mortality observed at lowest test concentration of 0.180 mg a.i./L and above.	42747902 (Acceptable)	Highly toxic
	Chronic	Mysid shrimp (*Americamysis bahia*)	**NOAEC: 0.0856 mg a.i./L** LOAEC: >0.0856 mg a.i./L No effects reported at any level. Water quality issues (a maximum pH of 9.98 was reported at the nominal 20 ug a.i./L treatment level).	47968901 (Supplemental)	N/A
Aquatic Plants	Non vascular	Green algae *(Selenastrum capricornutum)*	120-hr **EC_{50}: 0.83 mg a.i./L** **NOAEC= 0.56 mg a.i./L** based on cell density.	41984801 (Acceptable)	N/A
	Vascular	No Data	---	---	---

[1] Acute data for fathead minnow was requested in Table 11 below to provide data for determination of an ACR.

[2] Estimated from the mysid acute and chronic toxicity data and the daphnid acute data using the acute to chronic ratio (ACR) [0.24/0.0856 x 11/x; x=3.9]

Table 8. Summary of the Most Sensitive Endpoints from Terrestrial Toxicity Studies for Myclobutanil

Taxonomic Group	Study type	Surrogate Species	Toxicity	MRID (classification)	Acute Toxicity Classification
Birds	Acute	Bobwhite quail (*Colinus virginianus*)	Acute **LD_{50}: 498 mg a.i./kg-bw** NOAEL: not determined LOAEL= 316 mg/kg (lethargy and anorexia). Mortalities at all dose levels (1, 4, 8, 10 and 10, respectively). Good dose response.	00144286 (Acceptable)	Slightly toxic
	Subacute	Mallard (*Anas platyrhynchos*)	Subacute dietary **LC_{50} >4090 mg a.i./kg-diet** NOAEC= 1250 mg a.i./kg-diet LOAEC= 2220 mg a.i./kg-diet (anorexia and lethargy). One bird died at 4090 mg a.i./kg-diet.	00144288 (Acceptable)	Slightly toxic
	Chronic	Bobwhite quail (*Colinus virginianus*)	**NOAEC= 256 mg a.i./kg-diet** LOAEC >256 mg a.i./kg-diet No treatment-related effects at any level. Maximum exposure levels less than the predicted EECs.	43087901 (Supplemental)	N/A
Mammals[1]	Acute	Laboratory mouse (*Mus musculus*)	**LD_{50}= 1360 mg a.i./kg bw** Mortality at all dose levels tested. Multiple clinical signs, including ataxia, tremors, loss of righting and others – not dose-related; however, early deaths may have affected reporting.	00165239 (Acceptable)	Slightly toxic
	Acute	Laboratory rat *(Rattus norvegicus)*	LD_{50}= 1600 mg a.i./kg bw (M)	00141662 (Acceptable)	Slightly toxic
	Chronic	Laboratory rat (*Rattus norvegicus*)	**NOAEC (NOAEL)= 200 mg a.i./kg-diet (16 mg/kg bw/day)** LOAEC (LOAEL)=1000 mg a.i./kg-diet (80 mg/kg bw/day) -testicular, epididymal and prostatic atrophy in P2 males; slight increase in stillborns, decrease in body weight gain	00149581/ 00143766 (Acceptable)	N/A

Taxonomic Group	Study type	Surrogate Species	Toxicity	MRID (classification)	Acute Toxicity Classification
			in pups during lactation in F1 and F2 generations		
Terrestrial Invertebrates	Acute	Honey bee (*Apis mellifera L.*)	Contact LD_{50} > 100 µg a.i./bee	00144289 (Acceptable)	N/A

[1] Toxicity data for the oral mouse study was more sensitive than the rat study (oral mouse dose converts to a rat equivalent dose of 665 mg/kg bw). Rat data was included as this endpoint was used in HED assessments and for comparison to degradate toxicity data where rat was more sensitive than mouse in acute oral study (see Table 9).

Table 9. Summary of the Most Sensitive Data for each taxa for Myclobutanil Degradates (1,2,4-triazole, triazole alanine and triazole acetic acid)[1]

Taxonomic Group	Study type	Surrogate Species	Toxicity	MRID (classification)	Comments
1,2,4-triazole (aquatic toxicity)					
Freshwater fish	Acute	Rainbow Trout (*Oncorhynchus mykiss*)	96 hr-LC_{50} = 498 mg ai/L NOAEC = 378 mg ai/L (mortality)	48474301 (Acceptable)	None
	Chronic (28 day growth toxicity test)	Rainbow trout (*Oncorhynchus mykiss*)	LC_{50}: > 100 mg/L NOAEC (growth) ≥ 100 mg/L NOAEC (sublethal effects) = 3.2 mg/L LOAEC (sublethal effects) = 10.0 mg/L Observed sublethal effects included multiple fish being inactive or displaying abnormally low activity, labored respiration, and lying inactive on the bottom of the aquarium in the three highest	45880405 (Supplemental)	Supplemental due to non-guideline study

Taxonomic Group	Study type	Surrogate Species	Toxicity	MRID (classification)	Comments
			concentrations tested between days 23 and 28.		
Freshwater Invertebrates	Acute	Water flea (*Daphnia magna*)	LC_{50} = 900 (730 to 2200, 95% C.I.) mg/L.	00133381	Under Review
	Acute	Water flea (*Daphnia magna)*	48-hr EC_{50} > 98.1 mg ai/L NOAEC = 98.1 mg ai/L (based on mobility, highest concentration tested)	48453206 (Acceptable)	None
Aquatic Plants - Non vascular	Acute	Freshwater Algae (*Pseudokirchneriella subcapitata,* formerly *Selenastrum capricornutum*)	96-hr endpoints: <u>Biomass (most sensitive):</u> EC_{50} = 14 mg ai/L NOAEC = 3.1 mg ai/L <u>Cell Density:</u> EC_{50} = 18 mg ai/L NOAEC = 6.8 mg ai/L <u>Growth Rate:</u> EC_{50} > 31 mg ai/L NOAEC = 6.8 mg ai/L	45880401 (Acceptable)	None
	Acute	Green algae (*Scenedesmus subspicatus*)	EC_{50} = 6.3 (5.5 to 7.1, 95% C.I.) mg/L	00133382	Under Review
1,2,4-triazole (terrestrial toxicity)					
Birds	Acute	Coturnix quail *(Coturnix japonica)*	LD_{50} >316 mg/kg bw	45284015	Under Review
	Acute	Bobwhite quail (*Colinus virginianus*)	LD_{50} = 770 mg/kg bw NOAEL = 245 mg/kg bw LOAEL = 392 based on reduced body weight and food consumption; other observed effects included mortality	49380701 (Acceptable)	None

Taxonomic Group	Study type	Surrogate Species	Toxicity	MRID (classification)	Comments
			and clinical signs of toxicity		
Mammals	Acute	Laboratory mouse *(Mus musculus)*	LD_{50} = 3650 mg/kg	45284001	Review not available[2]
	Acute	Laboratory Rat (M) *(Rattus norvegicus)*	LD_{50} = 1375 mg/kg LD_{50} = 1648-3080 mg/kg	45284008 45284004, 45284001	Reviews not available[2]
	Reproduction and fertility effects 0, 250, 500, 3000 ppm M: 15, 31, 189 mkd F: 18, 36, 218 mkd	Laboratory rat *(Rattus norvegicus)*	<u>Parental:</u> NOAEC/NOAEL <250 ppm/15 mg/kg/day LOAEC/LOAEL= 250 ppm/15 mg/kg/day based on decrease in bodyweight, bodyweight gain and spleen weight. <u>Offspring:</u> NOAEC/NOAEL= <250 ppm/19 mg/kg/day LOAEC/LOAEL= 250 ppm/19 mg/kg/day based on decrease in bodyweight, bodyweight gain, brain and spleen weights <u>Reproduction:</u> NOAEC/NOAEL= 250 ppm/15 mg/kg/day Repro LOAEC/LOAEL= 500 ppm/31 mg/kg/day based on abnormal sperm and ↓# of corpus luteum (CL) in F_1 females At 3000 ppm/218 mg/kg/day, reproductive failure (no viable offspring), ↑CL in F_0 parental females	46467304 (Acceptable)	None

Taxonomic Group	Study type	Surrogate Species	Toxicity	MRID (classification)	Comments
	Developmental Toxicity in Rabbits 0,5,15,30,45 mg/kg/day	New Zealand white rabbit	<u>Parental/ Developmental:</u> NOAEL= 30 mg/kg/day LOAEL= 45 mg/kg/day based on mortality and clinical signs (decreased motor activity, head tilt, lacrimation, drooping eyelids, diarrhea and salivation) for parental effects and decreased fetal weight and urinary tract malformations for developmental effects Mortality (6/25 rabbits) in 45 mg/kg/day group	46492903 (Acceptable)	None
Terrestrial Invertebrates	Acute and reproductive (28 days)	Collembolan (springtails) Species (*Folsomia candida)* soil arthropods	LC_{50}>10 mg/kg NOAEC (mortality) ≥ 10mg/kg NOAEC (reproduction) = 1.8 mg/kg	45880404 (Supplemental)	Non-guideline study
	Growth and reproductive (8 weeks, adult 28 day exposure, additional 4 week offspring exposure)	Earthworms (*Eisenia fetida)*	LC_{50}> 70.81 ug/kg NOAEC ≥ 70.81 ug/kg (highest concentration tested) No significant treatment effects for mortality, behavior, body weights, reproduction or food consumption	45880402 (Supplemental)	Non-guideline study
Triazole alanine (aquatic toxicity)					
No submitted data identified					
Triazole alanine (terrestrial toxicity)					

Taxonomic Group	Study type	Surrogate Species	Toxicity	MRID (classification)	Comments
Mammals	90-day oral toxicity in rodents – rat 0, 1250, 5000, 20000 ppm M: 0, 90, 370, 1510 mg/kg/day F: 0,160, 400, 1680 mg/kg/day	Laboratory rat *(Rattus norvegicus)*	NOAEL = 90/160 mg/kg/day (M/F) LOAEL = 370/400 mg/kg/day (M/F) based on decreased leukocyte counts and decreased triglycerides in females At 1510/1680 mg/kg/day (M/F) decreased body weight (M), body weight gain (M), leukocytes (M/F) and triglycerides (M/F)	00164107 (Acceptable)	None
	Reproduction and fertility effects 0, 200, 2000, 10000 ppm M: (F0/F1) 0, 50/47, 213/192, 1098/929 mg/kg/day F: 0, 51/49, 223/199, 1109/988 mg/kg/day	Laboratory rat *(Rattus norvegicus)*	Parental: NOAEC/NOAEL= 10000 ppm/929 mg/kg/day LOAEC/LOAEL: >10000 ppm/929mg/kg/day Offspring: NOAEC/NOAEL <250 ppm/19 mg/kg/day LOAEC/LOAEL=2000ppm/192 mg/kg/day based on reduced mean litter weights in both generations Reproduction: LOAEC/LOAEL>10000 ppm/929mg/kg/day	00164112 (Acceptable)	None
Triazole acetic acid (aquatic toxicity)					
Freshwater Fish	Acute	Rainbow trout (*Oncorhynchus mykiss*)	96 hr-LC_{50} >101 mg ai/L NOAEC = 101 mg ai/L (mortality/sub-lethal effects)	48453209 (Acceptable)	None
Freshwater Invertebrates	Acute	Water flea (*Daphnia magna)*	48-hr EC_{50} > 108 mg ai/L NOAEC = 108 mg ai/L	48453208 (Acceptable)	None

Taxonomic Group	Study type	Surrogate Species	Toxicity	MRID (classification)	Comments
			(based on mobility, highest concentration tested)		
Triazole acetic acid (terrestrial toxicity)					
Mammals	Acute	Laboratory rat *(Rattus norvegicus)*	LD_{50} > 5000 mg/kg	45596802	Review not available[2]
	14 day oral toxicity in rodents 0, 100, 1000, 8000 ppm M: 0, 10.6, 102.8, 788.3 mg/kg/day F: 0, 10.1, 97.2, 703.5 mg/kg/day	Laboratory rat *(Rattus norvegicus)*	NOAEL = 788.3/703.5 mg/kg/day (M/F) LOAEL >788.3/>703.5 mg/kg/day (M/F)	45596801	None

1 Many endpoints derived from summary document USEPA 2006 b. 1,2,4-Triazole, Triazole Alanine, Triazole Acetic Acid: Human Health Aggregate Risk Assessment in Support of Reregistration and Registration Actions for Triazole-derivative Fungicide Compounds.

2 Values taken from triazole aggregate study referenced above, where it was noted that some values were from submitted summary data and full study reports were not available.

Exposure Pathways of Concern

The exposure pathways for myclobutanil and its transformation products may result in a wide range of potential aquatic and terrestrial exposure scenarios. For this problem formulation, the drinking water and inhalation pathways for birds and mammals were screened using the SIP (Screening Imbibition Program) and STIR (Screening Tool for Inhalation Risk) screening methods. STIR found the inhalation pathway not likely to be significant but the SIP analysis identified exposure through drinking water alone to be a potential concern for birds (acute and chronic) and mammals (chronic only). This is primarily due to the high water solubility of the compound and is a route of exposure that will be further analyzed in the forthcoming risk assessment.

It is also noted that these screening analyses do not include aggregation with all other exposure pathways (dietary, dermal, inhalation, or drinking water), which, together, may contribute to a total exposure that has a potential for effects to non-target animals. The risk characterization section will discusses the impact of the consideration of other routes of exposure that have been identified as potentially important, and the degree of certainty associated with screening-level risk assessment conclusions. SIP and STIR are described in detail at http://www.epa.gov/oppefed1/models/terrestrial/index.htm and the SIP and STIR model inputs and outputs for myclobutanil are available in **Appendices B** and **C**, respectively.

3. ANALYSIS PLAN

Drinking Water Assessment

An updated drinking water assessment will be conducted to support future human health dietary risk assessments of myclobutanil, as well as an updated aggregate drinking water assessment for triazole-derivative fungicides. Such an assessment is needed because the fate half-lives calculated for this problem formulation in accordance with recent guidance (USEPA 2012 c.,d.) are likely to alter drinking water exposure estimates. The drinking water assessment will incorporate model estimates of myclobutanil and any additional transformation products to those previously identified by the Health Effects Division as residues of toxicological concern in surface water and groundwater. The registration review drinking water assessment will include modeling results as well as a summary of available surface water and groundwater monitoring data, if available.

The current model for conducting drinking water assessments for surface water is the Surface Water Concentration Calculator (SWCC). In the absence of newer models approved within OPP, it is expected that SWCC will be used to simulate pesticide transport as a result of runoff and erosion from an agricultural field and to estimate environmental fate and transport of pesticides in the index reservoir. Measures of exposure will be based on maximum single and year (including multiple seasons per year) labeled application rates, minimum retreatment intervals, and conservative methods of application.

Currently, groundwater modeling is completed using PRZM-Groundwater (PRZM-GW). PRZM-GW is used to simulate vertical pesticide transport through the soil profile into an aquifer following application to an agricultural field. The PRZM scenarios used in groundwater simulations are representative of vulnerable sites—shallow unconfined aquifers under an agricultural field with leaching prone soil—and output values represent pesticide concentrations that may be observed in drinking water resulting from the use of groundwater vulnerable to pesticide contamination as source water. The results are expected to represent the upper bound values on the concentrations of toxic residues that might be found in drinking water supplied by groundwater.

Ecological Risk Assessment

Stressors of Concern

Toxicity data for the primary degradate of concern 1,2,4-triazole as well as its conjugates (1,2,4-triazole alanine and 1,2,4-triazole acetic acid) are presented in **Table 6**. Only the 1,2,4-triazole degradate was considered a major degradate based on soil and water metabolism studies for myclobutanil; however, 1,2,4-triazole acetic acid was a major degradate in fate studies conducted for 1,2,4-triazole, and there is evidence that 1,2,4-triazole and the triazole conjugates can interconvert in soil and aquatic systems. (USEPA, 2006 a.). In addition to environmental degradates of concern, plant and mammalian metabolites of concern of myclobutanil include 1,2,4-triazole, 1,2,4-triazole alanine, 1,2,4-triazole acetic acid and RH-9090 [α-(3-hydroxybutyl)-α-(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile]. In addition to 1,2,4-triazole acetic acid, hydroxytriazole was identified as a major transformation product of 1,2,4-triazole. Based on myclobutanil's persistence in soil and water, it is considered unlikely that hydroxytriazole will reach levels greater than 10% of the parent compound in the environment. No toxicity data were available for hydroxytriazole.

Based on review of toxicity studies available for 1,2,4-triazole, 1,2,4- triazole alanine and 1,2,4-triazole acetic acid, these degradates appear to generally show similar or less toxicity to aquatic or terrestrial organisms than the parent compound, myclobutanil. In general, aquatic species appear to be less sensitive to the degradates, whereas birds and mammals tend to show similar toxicity. Previous documents (USEPA, 2006 b., Duah, et al. 2001) referenced an oral rabbit study with an LD_{50} of 666 mg/kg/day for 1,2,4-triazole but the study results could not be substantiated with the available literature (MRID cited did not contain an oral rabbit study). There has been some concern raised in other discussions (USEPA 2006 b., Duah, et al. 2001) about the possible increased sensitivity of rabbits to the triazole degradates based on the reported oral LD_{50} of 666 mg/kg/day and mortality seen at 45 mg/kg/day in the neurodevelopmental study (MRID 46492903).

Although no toxicity studies are available for the metabolite RH-9090, this compound is considered to be of equivalent toxicity to the parent based on the structural activity relationship (SAR) (USEPA, 2006 b.). In addition, tolerances for myclobutanil residues in food are established for the combined residues of myclobutanil and RH-9090 on registered commodities. For the degradates of concern, ECOSAR (Ecological Structure Activity Relationship), v1.11, and SMILES Codes were used to assess their toxicity relative to the parent compound myclobutanil and aquatic organisms. Predicted values from ECOSAR for the parent compound myclobutanil were generally in agreement with the toxicity study results, indicating ECOSAR may be useful for estimating degradate toxicity. The ECOSAR analysis indicated lower predicted toxicity for each of the degradation products than the parent, including the degradate hydroxytriazole, for which no toxicity data were available. Results of this analysis as well as a summary table comparing toxicity study endpoints for myclobutanil and its degradates are included in **Appendix D**.

Previous assessments have used a Total Toxic Residue (TTR) approach for assessing ecological and drinking water risks for myclobutanil and residues of concern in the absence of empirical toxicity data for the degradates. This modeling strategy uses the assumption that all residues of concern have similar physical, chemical, and partitioning characteristics as well as equal or less toxicity than the parent compound. Based on the review of the toxicity studies available on the degradation products and ECOSAR analysis, it is anticipated that the TTR approach will not be necessary for the aquatic ecological assessment and only the parent compound will be considered due to the lower toxicity of the degradates compared to the parent. However, as myclobutanil and its transformation products of concern have generally equivalent toxicity for birds and mammals, degradates would be considered as part of the terrestrial assessment for these species by using a conservative foliar half-life for the terrestrial analysis.

Measures of Exposure

In order to estimate risks of myclobutanil exposure to aquatic and terrestrial organisms, all exposure modeling and resulting risk conclusions will be made based on maximum application rates, application methods, and any mitigation measures specifically indicated on the label. The models that will be used to predict the estimated environmental concentrations (EECs) of myclobutanil are discussed on OPP's model website http://www.epa.gov/opp00001/science/models_pg.htm. In addition, E-FAST and any additional available exposure models may be used to assess use in drains, drain lines, irrigation supply systems, waste water systems, sewage systems, sewer lines, and storm sewers. E-FAST is described in detail at http://www.epa.gov/oppt/exposure/pubs/efast.htm.

The registration review preliminary risk assessment may include modeling exposures for some crops to account for the multiple crop cycles or crop rotations that may occur within a given calendar year which may not have been previously considered.

The Agency is also aware of monitoring conducted by federal and state agencies and this route of exposure will be considered in the assessment to the extent that data on myclobutanil and 1,2,4-triazole are available.

Measure of Effects

Ecological effects data are used as measures of direct and indirect effects to biological receptors. Data are typically obtained from registrant-submitted studies and from literature studies identified by ECOTOX. The ECOTOX database provides more ecological effects data in an attempt to bridge existing data gaps. ECOTOX is a source for locating single chemical toxicity data and potential chemical mixture toxicity data for aquatic life, terrestrial plants, and wildlife. ECOTOX was created and is maintained by the U.S. EPA, Office of Research and Development, and the National Health and Environmental Effects Research Laboratory's Mid-Continent Ecology Division. Deficiencies were identified in the available toxicology data submitted to date from the registrant, including data gaps based on new guidelines or concern about species sensitivities. These are outlined in Tables 11 and 12 below.

Integration of Exposure and Effects

Risk characterization is the integration of exposure and ecological effects to determine the potential ecological risk from the use of pesticides and the likelihood of direct and indirect effects to non-target organisms in aquatic and terrestrial habitats. For the assessment of risks, the risk quotient (RQ) method is used to compare exposure and measured toxicity values. EECs are calculated for acute and chronic concentrations and are compared to acute and chronic toxicity endpoints. The resulting RQs are then compared to the Agency's Levels of Concern (LOCs) (USEPA 2004). These criteria will be used to indicate when myclobutanil use, as directed on the label, has the potential to cause adverse direct effects to non-target organisms. In addition, any available incident data will be considered (see below) as part of the risk characterization.

Endangered Species Assessments

In November 2013, the EPA, along with the U.S. Fish & Wildlife Service (USFWS), the National Marine Fisheries Service (NMFS) (collectively, the Services), and the U.S. Department of

Agriculture (USDA) released a summary of their joint Interim Approaches for assessing risks to listed species from pesticides. The Interim Approaches were developed jointly by the agencies in response to the National Academy of Sciences' (NAS) recommendations and reflect a common approach to risk assessment shared by the agencies as a way of addressing scientific differences between the EPA and the Services. The NAS report outlines recommendations on specific scientific and technical issues related to the development of pesticide risk assessments that EPA and the Services must conduct in connection with their obligations under the Endangered Species Act (ESA) and FIFRA. The joint Interim Approaches were released prior to a stakeholder workshop held on November 15, 2013. In addition, the EPA presented the joint Interim Approaches at the December 2013 Pesticide Program Dialogue Committee (PPDC) and State-FIFRA Issues Research and Evaluation Group (SFIREG) meetings, and held a stakeholder workshop in April 2014, allowing additional opportunities for stakeholders to comment on the Interim Approaches. As part of a phased, iterative process for developing the Interim Approaches, the agencies will also consider public comments on the Interim Approaches in connection with the development of upcoming Registration Review decisions. The details of the joint Interim Approaches are contained in the white paper "Interim Approaches for National-Level Pesticide Endangered Species Act Assessments Based on the Recommendations of the National Academy of Sciences April 2013 Report," dated November 1, 2013.

Given that the agencies are continuing to develop and work toward implementation of the Interim Approaches to assess the potential risks of pesticides to listed species and their designated critical habitat, the ecological risk assessment supporting the proposed interim registration review decision for myclobutanil is not expected to contain a complete ESA analysis. Once the agencies have fully vetted the scientific methods necessary to complete risk assessments for endangered and threatened (listed) species and their designated critical habitats, these methods will be applied to subsequent analyses for myclobutanil as part of completing this registration review.

Endocrine Disruptor Screening Program

As required by FIFRA and FFDCA, EPA reviews numerous studies to assess potential adverse outcomes from exposure to chemicals. Collectively, these studies include acute, subchronic and chronic toxicity, including assessments of carcinogenicity, neurotoxicity, developmental, reproductive, and general or systemic toxicity. These studies include endpoints which may be susceptible to endocrine influence, including effects on endocrine target organ histopathology, organ weights, estrus cyclicity, sexual maturation, fertility, pregnancy rates, reproductive loss, and sex ratios in offspring. For ecological hazard assessments, EPA evaluates acute tests and chronic studies that assess growth, developmental and reproductive effects in different taxonomic groups. As part of registration review for myclobutanil, EPA will review these data and select the most sensitive endpoints for relevant risk assessment scenarios from the existing hazard database. However, as required by FFDCA section 408(p), myclobutanil is subject to the endocrine screening part of the Endocrine Disruptor Screening Program (EDSP).

EPA has developed the EDSP to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine-related effects caused by the substance, and establish a dose-response relationship between the dose and the E, A, or T effect.

Under FFDCA section 408(p), the Agency must screen all pesticide chemicals. Between October 2009 and February 2010, EPA issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. A second list of chemicals identified for EDSP screening was published on June 14, 2013[1] and includes some pesticides scheduled for registration review and chemicals found in water. Neither of these lists should be construed as a list of known or likely endocrine disruptors.

Myclobutanil is on List 1 for which EPA has received all the required Tier 1 assay data. The Agency is currently reviewing all of the assay data received for the appropriate List 1 chemicals and planning to make the conclusions of those reviews available in early 2015. For further information on the status of the EDSP, the policies and procedures, the lists of chemicals, future lists, the test guidelines, and the Tier 1 screening battery, please visit our website.[2]

[1] See http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0477-0074 for the final second list of chemicals.

[2] http://www.epa.gov/endo/

Review of Incident Data

Three incident databases are available: 1) the Ecological Incident Information System v. 2.1.1 (EIIS), maintained by EFED; 2) the Avian Incident Monitoring System (AIMS), maintained by the American Bird Conservancy; and, 3) the Incident Data System (IDS) maintained by OPP. These databases were searched on 11/12/14.

The Ecological Incident Information System (EIIS) database was queried for incidents related to myclobutanil use. Four incidents were reported in the EIIS database, three with effects on terrestrial plants (two incidents with grapes and one with roses) and one on aquatic species (both fish and invertebrates). The two incidents with grapes occurred in California and the one with roses was reported in Maryland. The certainty index for the damage in all 3 incidents to plants was rated as possibly related to exposure to myclobutanil. The two incidents with grapes involved application of other pesticides as well as the myclobutanil. Therefore, it is not definitively known whether or not the effects were due to exposure to myclobutanil in these two incidents. Myclobutanil was the only pesticide applied to the rose bushes in the third plant reported incident. In the fourth incident involving aquatic species, the incident was rated as highly probable. However, one other pesticide was involved in this incident; therefore, it is not definitely known whether or not the effects were due to myclobutanil exposure.

Incident 1: On May 30, 1994, Rally 40W (myclobutanil), Pro Gibb (gibberellic acid), dimethogan 25 WP, Pro Kil Cryolite 96 (sodium fluoaluminate), Britz binder and Booster 42

Foliar Spray (polymeric polyhydroxy acids) were applied by ground application to grape vines. Shortly after the last application, scarring of the berries, stunted vine growth, lack of berry size increase, dieback of fruit from total bunches and limited cone growth with straggly branches were observed. No residue analysis was conducted. The California Commissioner's report indicated that mixtures of Pro-Gibb 4% and Pro-Kil Cryolite 96 may have caused some compatibility problems. No specific data on terrestrial plants were found in the Agency files for any of the pesticides applied on this incident.

Incident 2: On June 2, 2000, it was reported that Rally 40W damaged 6 acres of Red Globe and Thompson's grapes to the extent that they were unfit for sale. Burns and necrosis on bunches (Red Globe) and leaf burn (Thompson's) were observed. Agri-MEK (abamectin) and Ad-Wet were also applied, using a ground spray on the vineyard. No plant tissue or environmental samples were found in the Agency files for any of the pesticides applied in this incident.

Incident 3: On June 16, 2003, Systhane (myclobutanil) was applied via a broadcast spray to rose bushes grown in greenhouses by local residents in Maryland. The total magnitude was 200 houses. Foliar necrosis and some defoliation were observed after exposure to Systhane. Damage varied from house to house and by rose variety. No plant tissue or environmental samples were collected for this incident.

Incident 4: On July 28, 2009, an investigator for the Iowa Department of Natural Resources visited a grower who was concerned an airplane may have applied or may have allowed a pesticide application to drift into Flint Creek in Des Moines County, IA. The inspector observed dead and dying crayfish in the creek. Freshwater bluegill were also found dead. The active ingredients chlorpyrifos and myclobutanil were detected in bluegill tissue samples.

A query of the aggregate Incident System (IDS) on 11/12/2014 reported 29 incidents to plants (dates ranging from 1998-2012).

The Avian Incident Monitoring System (AIMS), a database administered by the American Bird Conservancy, was queried for myclobutanil on 11/12/2014 and to date, there were no bird incidents reported.

The absence of documented incidents in these databases does not necessarily mean that such incidents did not occur. Mortality incidents must be seen, reported, investigated, and submitted to the Agency in order to be recorded in the incident databases. In addition, incident reports for non-target organisms typically provide information only on mortality events and plant damage. Sublethal effects in organisms such as abnormal behavior, reduced growth and/or impaired reproduction are rarely reported, except for phytotoxic effects in terrestrial plants.

Uncertainties

- As previously discussed, many of the labels do not specify the maximum number of applications that can be applied per year or crop cycle and/or the number of crop cycles per year. Some labels are missing a single maximum application rate. We request that in completing the Use Pattern Summary Table, the registrants provide this information.

4. PRELIMINARY IDENTIFICATION OF DATA GAPS

Environmental Fate

Table 10 identifies the environmental fate studies by MRID that offer data for each Part 158 data requirement, as well as study classifications and whether or not further data are anticipated to be needed in order to support risk assessment for the myclobutanil registration review. Although no additional fate and transport data are being requested for myclobutanil under registration review, the table indicates studies for which data voluntarily submitted by the registrant may assist in refining the assessment. No additional data for 1,2,4-triazole or its conjugates are needed to conduct the myclobutanil drinking water or ecological risk assessments under registration review.

Table 10. Submitted Environmental Fate Data for Myclobutanil

OCSPP Guideline	Data Requirement	Submitted Studies (MRID)	Study Classifications	Are data needed?	Additional Comments
835.2120	Hydrolysis	00141679	Acceptable	No	None
835.2240	Aqueous photolysis	00164560 40641501 40319801 40528801	Acceptable in combination	No	Not requesting data but any additional studies submitted voluntarily would help refine the assessment
835.2410	Soil photolysis	00164987 00164988	Acceptable in combination	No	None
835.4100	Aerobic soil metabolism	00141680 00164561	Individual study acceptable	No	Not requesting data but any additional studies submitted voluntarily would help refine the assessment
835.4200	Anaerobic soil metabolism	00141680 00164561	Individual study acceptable	No	Not requesting data but any additional studies submitted voluntarily would help refine the assessment
835.4300	Aerobic aquatic metabolism	47454401	Acceptable	No	None
835.4400	Anaerobic aquatic metabolism	No data		No	Not requesting data but any additional studies submitted voluntarily would help refine the assessment
835.1230	Adsorption/ desorption	00141682	Supplemental	No	None
835.1410	Volatility – laboratory	No data		No	Not triggered based on low vapor pressure ($7.07X10^{-9}$ torr at 25°C)
835.6100	Terrestrial field dissipation	00164563 00164987	Acceptable	No	None

OCSPP Guideline	Data Requirement	Submitted Studies (MRID)	Study Classifications	Are data needed?	Additional Comments
835.6200	Aquatic field dissipation	No data		No	Not triggered based on exposure aquatic toxicity profile.
850.1730	Fish bioconcentration	No data		No	Low K_{ow} indicates a low potential for bioaccumulation.
850.6100	Analytical method in soil	No data		No	All field dissipation studies were conducted prior to April 19, 1996; therefore, Environmental Chemistry Method (ECM) and Independent Laboratory Validation (ILV) data are not required.
850.6100	Analytical method in water	No data		No	

Ecological Effects

Tables 11 and 12 identify the ecological effects studies, as well as study classifications, and whether or not further data are anticipated to be needed in order to support risk assessment for registration review. The rationale for the additional data that EFED recommends be requested is presented within the tables.

Table11. Submitted Aquatic Ecological Effects Data for Myclobutanil

OCSPP Guideline	Data Requirement Test Material	Submitted Studies (MRID)	Study Classifications	Are data needed for risk assessment?	Comments
850.1010	Freshwater invertebrate acute toxicity	00141678	Acceptable	No	None
850.1025 850.1035	Estuarine/saltwater invertebrate acute toxicity	42747901	Supplemental	No	Controls did not meet the minimum shell growth requirement of 2 mm (1.4-1.5 mm control shell growth reported) in the eastern oyster study (MRID 42747901). Based on a review of data from other conazoles, mysid shrimp has predominantly been a more sensitive species than the eastern oyster and toxicity values were generally similar. As an acceptable mysid shrimp study is available, a new oyster study is not requested at this time.
		42747902	Acceptable	No	See above
850.1075	Freshwater fish acute toxicity TGAI	00144285	Acceptable	**Yes**	Under Guideline 850.1400, a 96-hour LC_{50} is required for the test species used in the freshwater early life stage study (fathead minnow). There is uncertainty with the available freshwater fish acute toxicity endpoint being the most sensitive species. Based on the most sensitive chronic fish study, it is recommended that the study be conducted using the fathead minnow.
850.1075	Saltwater fish acute toxicity	42747903	Acceptable	No	None
850.1300	Freshwater invertebrate life cycle	No data		No	NOAEC estimated using ACR for mysid shrimp acute and chronic toxicity data

OCSPP Guideline	Data Requirement Test Material	Submitted Studies (MRID)	Study Classifications	Are data needed for risk assessment?	Comments
850.1350	Estuarine/saltwater invertebrates life cycle	47968901	Supplemental	No	Estimated EECs based on the label application rates and frequency are expected to exceed the upper limit of toxicity testing for this study. In the absence of additional toxicity data at higher dose ranges, the NOAEC of 0.0856 mg a.i./L will be used. Although protective, this could have implications for future endangered species assessments due to the conservative nature of the endpoint and could lead to overly conservative risk assumptions.
850.1735	Benthic invertebrates (acute)	No data		No	Not triggered per 40 CFR Part 158 based on chemical characteristics
850.1740	Benthic invertebrates (chronic)	No data		No	Not triggered per 40 CFR Part 158 based on chemical characteristics–
850.1400	Freshwater fish early-life stage	00164986/ 40409201/ 40480401	Acceptable	No	As per 40 CFR, if a different test species is used for the chronic (early-life stage) data requirement than the acute study, a 96 hour LC_{50} must be provided. If the acute study (850.1075) is repeated with the fathead minnow as previously discussed, this requirement is fulfilled and an additional chronic study is not needed.

OCSPP Guideline	Data Requirement Test Material	Submitted Studies (MRID)	Study Classifications	Are data needed for risk assessment?	Comments
850.1400	Estuarine/saltwater fish early-life stage	No data		No	If data are provided as mentioned regarding the 850.1400/850.1075 studies, NOAEC can be estimated using ACR for freshwater fish acute and chronic toxicity data in lieu of providing this study.
850.1500	Fish life cycle	No data		No	Study not needed if 850.1400 requirements for freshwater and saltwater fish are fulfilled.
850.4400	Aquatic plant Toxicity Test Using Lemna spp. TEP	No data		**Yes**	No toxicity data are available for myclobutanil to address risks to vascular plants. Multiple incident reports have involved myclobutanil and plant species.
850.4500	Algal Toxicity TEP	41984801	Acceptable	**Yes**	Guidance recommends testing on four of the most sensitive nonvascular organisms whereas submitted data only includes one. Multiple incident reports have involved myclobutanil and plant species.
850.4550	Cyanobacteria (Anabaena flos-aquae) Toxicity TEP	No data		**Yes**	

Table 12. Submitted Terrestrial Ecological Effects Data for Myclobutanil

OCSPP Guideline	Data Requirement Test Material	Submitted Studies (MRID)	Study Classifications	Are data needed for risk assessment?	Comments
850.2100	Avian oral toxicity	00144286	Acceptable	**Yes**	

OCSPP Guideline	Data Requirement Test Material	Submitted Studies (MRID)	Study Classifications	Are data needed for risk assessment?	Comments
	TGAI		No data for passerine		Based on effects noted in the available toxicity data, and the potential for passerines to be more sensitive than the species previously tested, EFED recommends requesting a passerine study.
850.2200	Avian dietary toxicity	0144288	Acceptable	No	None
850.2300	Avian reproduction	43087901	Supplemental	No	Estimated EECs based on the label application rates and frequency are expected to exceed the upper limit of toxicity testing for the avian reproduction study. In the absence of additional toxicity data at higher dose ranges, the NOAEC of 256 mg a.i./kg diet will be used to estimate risks. Although protective, this could have implications for future endangered species assessments due to the conservative nature of the endpoint and could lead to overly conservative risk assumptions.
Non-guideline	Avian inhalation	No data		No	Based on STIR analysis, risks through inhalation pathway are not expected.
81-1	Acute mammalian oral LD_{50} (rat)	00165239/ 00141662	Acceptable	No	None
83-4	Mammalian Reproduction (rat)	00149581/ 00143766	Acceptable	No	None

OCSPP Guideline	Data Requirement Test Material	Submitted Studies (MRID)	Study Classifications	Are data needed for risk assessment?	Comments
850.3020	Honey bee adult acute contact toxicity	00144289	Acceptable	No	Tier 1 toxicity test.
850.3030	Honey bee toxicity of residues on foliage	None		No	This study is not triggered based on the reported endpoint in the honey bee adult acute contact study.
Non-guideline OECD TG 213	Honey bee adult acute oral toxicity TGAI	No data		Yes	Tier 1 toxicity test.
Non-guideline OECD TG 237	Honey bee larvae acute and chronic oral toxicity TGAI	No data		Yes	Tier 1 toxicity test.
Non-guideline	Honey bee adult chronic oral toxicity TGAI	No data		Yes	Tier 1 toxicity test.
Non-guideline OECD Guidance 75	Semi-field testing for pollinators TEP	No data		Yes	Tier 2 test contingent on results of tier 1 tests and screening level residues.
Non-guideline	Field trial of residues in pollen and nectar TEP	No data		Yes	Tier 2 test contingent on results of tier 1 tests and screening level residues.
850.3040	Field testing for pollinators TEP	No data		Yes	Tier 3 testing contingent on results of earlier tiers of testing.

OCSPP Guideline	Data Requirement Test Material	Submitted Studies (MRID)	Study Classifications	Are data needed for risk assessment?	Comments
850.4100	Terrestrial plant toxicity: Tier II seedling emergence TGAI	No data		Yes	No toxicity data are available for myclobutanil to address risks to terrestrial plants. Multiple incident reports have involved myclobutanil and plant species.
850.4150	Terrestrial plant toxicity: Tier II vegetative vigor TEP	No data		Yes	

Additional justification for non-guideline data requests:

Study Title: Honeybee Acute Oral Toxicity, Adult Non-guideline Study, OECD 213
Rationale for Requiring the Data
Terrestrial invertebrates are likely to be impacted if exposed to pesticides in various use settings. With eusocial bees, pesticide residues may be transferred to pollen and/or nectar of treated plants and subsequently brought back to the hive. Therefore, potential acute effects to adult honeybees and other insect pollinators from oral exposure to some pesticides could exist. Currently available toxicity studies do not address possible effects of oral exposure on adult terrestrial insect survival. Because of the potential for pollen and nectar to be contaminated with pesticide residues, and subsequently brought back to the hive, it is important to determine the acute oral toxicity of this compound to adult honeybees and other insect pollinators. The Office of Pesticide Programs has made available a guidance regarding ecological testing for bees using the honeybee as a surrogate test species. The guidances discusses Tier I laboratory-based acute oral toxicity studies of individual adult bees as a critical component of the screening-level risk assessment process for examining potential adverse effects from specific routes of exposure. The guidance can be found at: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance. Additional guidance on the honeybee oral toxicity test design can be found in OECD Test Guideline 213 (http://www.oecd-ilibrary.org/docserver/download/9721301e.pdf?expires=1423074617&id=id&accname=guest&checksum=2F0764FCB4DCF01D32382952A2E995C3)
Practical Utility of the Data
How will the data be used? The Tier 1 acute oral toxicity data on adult honeybees serve as a foundation for the screening-level assessment of potential risk non-target organisms such as federally listed threatened or endangered and non-listed terrestrial invertebrate insects, including pollinators, from acute oral exposures to pesticides. The data will be used to reduce uncertainties associated with the risk assessment for terrestrial invertebrates and will improve EPA's understanding of the potential direct and indirect effects on a broad range of taxa. This study will also provide information with which to compare whether oral toxicity estimates differ from contact toxicity estimates obtained from other Tier 1 studies. If acute oral effects data for adult honey bees are not available, risks to terrestrial insects from acute oral exposure will be assumed. **How could the data impact the Agency's future decision-making?** The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect listed threatened or endangered species and/or modify their designated critical habitat. Without these data, EPA may need to presume risk, which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in use restrictions.

Study Title: Honeybee Acute Oral Toxicity, Larvae Non-guideline Study, OECD 237
Rationale for Requiring the Data
Terrestrial invertebrates are likely to be impacted if exposed to pesticides in various use settings. With eusocial bees, pesticide residues may be transferred to pollen and/or nectar of treated plants and subsequently brought back to the hive where developing larvae and pupae may be exposed. Therefore, potential adverse effects to developing bees could result from exposure to pesticide residues. Available toxicity studies do not address possible effects on brood (larvae and pupae) survival/development. Because of the potential for pollen and nectar to be contaminated with pesticide residues, and subsequently brought back to the hive, it is important to determine the acute toxicity of this compound to bee brood. The Office of Pesticide Programs has made available a guidance regarding ecological testing for bees using the honeybee as a surrogate test species. The guidances discusses Tier I laboratory-based acute toxicity studies of individual honeybee larvae as a critical component of the screening-level risk assessment process for examining potential risks from specific routes of exposure. The guidance be found at: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance. Additional guidance on larval honeybee toxicity test design can be found in OECD Test Guideline 237 (http://www.oecd-ilibrary.org/docserver/download/9713171e.pdf?expires=1422485600&id=id&accname=guest&checksum=D8E07C2B1DF77BF096C3B29F55BF86A7). In some cases, information pertaining to acute toxicity to honey bee larvae may be obtained with the chronic honey bee larval test thereby negating the need for separate acute and chronic larval toxicity tests.
Practical Utility of the Data
How will the data be used? The Tier 1 acute toxicity data on honeybee larvae serve as a foundation for the screening-level assessment of potential risk to non-target organisms including federally listed threatened or endangered and non-listed terrestrial invertebrates, including pollinators, and/or modify their designated critical habitat from acute exposures to pesticides. The data will be used to reduce uncertainties associated with the risk assessment for terrestrial invertebrates and will improve EPA's understanding of the potential effects on terrestrial species and whether there is a differential sensitivity of larval bees relative to adult bees. If acute effects data for larvae are not available, risks to terrestrial insects from acute exposure will be assumed. **How could the data impact the Agency's future decision-making?** The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect listed threatened or endangered species and/or modify their designated critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in use restrictions.

Study Title: Pollinator Chronic Oral Toxicity, Adult **Non-guideline Study**
Rationale for Requiring the Data
Terrestrial invertebrates are likely to be impacted if exposed to pesticides in various use settings. With eusocial bees, pesticide residues may be transferred to pollen and/or nectar of treated plants and subsequently brought back to the hive. Therefore, potential chronic effects to adult honeybees and other pollinators from oral exposure to some pesticides could exist. Currently available toxicity studies do not address possible lethal and sublethal effects of chronic oral exposure on adult terrestrial invertebrates and will assist in determining whether the sensitivity of adult bees differs from that of earlier life stages. Because of the potential for pollen and nectar to be contaminated with pesticide residues, and subsequently brought back to the hive, it is important to determine the chronic oral toxicity of this compound to adult honeybees and other pollinators. The Office of Pesticide Programs has made available a guidance regarding ecological testing for bees using the honeybee as a surrogate test species. The guidances discusses Tier I laboratory-based chronic oral toxicity studies of individual adult honeybees as a critical component of the screening-level risk assessment process for examining potential risks from specific routes of exposure. The guidance can be found at: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance. Although study design elements for the chronic 10-day oral toxicity test with honey bees are similar to the OECD TG 213 acute oral toxicity test (http://www.oecd-ilibrary.org/docserver/download/9721301e.pdf?expires=1422484908&id=id&accname=guest&checksum=C38495D2A570AC2216CFB1F223D24AA7), EPA requests that the proposed protocol for this study be submitted for review and approval by EPA prior to initiating the test.
Practical Utility of the Data
How will the data be used? The Tier 1 chronic toxicity data on adult bees serve as a foundation for the screening-level assessment of potential risk to non-target organisms including federally listed threatened or endangered species and non-listed terrestrial invertebrates, including pollinators, from chronic oral exposures to pesticides. The data will be used to reduce uncertainties associated with the risk assessment for terrestrial invertebrates and will improve EPA's understanding of the potential direct and indirect lethal and sublethal effects on a broad range of terrestrial species, particularly insect pollinators and to determine whether adult toxicity differs substantially from other life stages evaluated in other Tier 1 tests. If chronic oral effects data for adults are not available, risks to terrestrial insects from chronic exposure will be assumed. **How could the data impact the Agency's future decision-making?** The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect listed threatened or endangered species and/or their designated critical habitat. Without these data, EPA may need to presume risk which will

limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in use restrictions.

Study Title: Pollinator Chronic Oral Toxicity, Larvae **Non-guideline Study**
Rationale for Requiring the Data
Terrestrial invertebrates are likely to be impacted if exposed to pesticides in various use settings. For eusocial bees, pesticide residues may be transferred to pollen and/or nectar of treated plants and subsequently brought back to the hive where larvae and pupae may be exposed. Therefore, potential effects to developing bees could result from chronic exposure to pesticide residues. Available toxicity studies do not address possible chronic effects on brood (larvae and pupae) survival. Because of the potential for pollen and nectar to be contaminated with pesticide residues, and subsequently brought back to the hive, it is important to determine chronic larval/pupal toxicity and whether adult emergence is adversely affected. This study will provide information on whether honeybee larvae differ in sensitivity from adult bees following chronic exposure. The Office of Pesticide Programs has made available a guidance regarding ecological testing for bees using the honeybee as a surrogate test species. The guidances discusses Tier I laboratory-based chronic toxicity studies of individual honeybee larvae as a critical component of the screening-level risk assessment process for examining potential risks from specific routes of exposure. The guidance can be found at: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance. Additional information on larval honeybee toxicity repeat exposure test design can be found in the OECD draft guidance (http://www.oecd.org/env/ehs/testing/Draft_GD_honeybees_rep_exp_for_2nd_CR_25_November_2013.pdf). Although study design elements for the chronic 21-day toxicity test with honey bee larvae have been drafted, EPA requires that the proposed protocol for this study be submitted for review and approval by EPA prior to initiating the test.
Practical Utility of the Data
How will the data be used? The Tier 1 chronic toxicity data on bee larvae serve as a foundation for the screening-level assessment of potential risk to non-target organisms including federally listed threatened or endangered and non-listed terrestrial invertebrates, including insect pollinators, from chronic exposures to pesticides. These data will be used to reduce uncertainties associated with the risk assessment for terrestrial invertebrates and will improve EPA's understanding of the potential direct and indirect lethal and sublethal effects on a broad range of terrestrial species, particularly insect pollinators. These data will also assist in determining whether early life stages of the bee differ in their sensitivity to pesticides relative to adults. If chronic effects data for larvae are not available, risks to terrestrial insects from chronic exposure will be assumed. **How could the data impact the Agency's future decision-making?**

The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect listed threatened or endangered species and/or modify their designated critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in use restrictions.

Study Title: Pollinator Tier II Semi-Field Toxicity Testing (tunnel/enclosure studies) **Non-guideline Study, OECD 75**
Rationale for Requiring the Data
Tier II studies are conditional on the outcome of the screening-level assessment where acute and/or chronic risk levels of concern have been exceeded for terrestrial invertebrates. Terrestrial invertebrates are likely to be impacted if exposed to pesticides in various use settings. For eusocial bees, pesticide residues may be transferred to pollen and/or nectar of treated plants and subsequently brought back to the hive and may adversely affect developing brood (egg, larvae, and pupae) and adult bees. Screening-level (Tier 1) studies of individual bees do not address possible effects and/or exposure to pesticide residues at the colony-level. Because of the potential for pollen and nectar to be contaminated with pesticide residues, and subsequently brought back to the hive, it is important to determine whether bee colonies may be negatively affected under relatively controlled exposure conditions of a semi-field study. In addition to providing effects data, these studies can provide data on pesticide residues in pollen/nectar of treated plants. The Office of Pesticide Programs has made available a guidance regarding ecological testing for invertebrates with the honeybee. The guidance describes the tiered testing process and can be found at: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance . Additional information on honeybee colony studies under semi-field conditions can be found in th OECD Guidance 75 http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono%28.
Practical Utility of the Data
How will the data be used? Tier II colony-level data will be used to assess potential risk to non-target organisms including listed and non-listed terrestrial social invertebrate species and to determine whether effects observed in the screening-level (Tier I) laboratory-based studies of individual bees are evident in colony-level studies under semi-field conditions. The Tier II semi-field test of whole colonies is a relatively controlled study, *i.e.*, bees are confined to a specific area, that is designed to represent potential field-level exposure and account for hive dynamics, which are not achievable from other pollinator studies. This study will be used to determine whether adverse effects to insect pollinators at the whole colony level, may result for the use of pesticides and will help to refine risk estimates derived in the screening-level risk assessment for beneficial terrestrial

invertebrates. Measured residues in pollen/nectar can also be used to refine risk estimates derived from model-based or default values in the screening-level assessment. **How could the data impact the Agency's future decision-making?** The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect federally listed threatened or endangered species or their designated critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in significant use restrictions.

Tier II Semi-Field Toxicity Testing for Pollinators (Feeding Studies)
Rationale for Requiring the Data
For eusocial bees, pesticide residues may be transferred to pollen and/or nectar of treated plants and subsequently brought back to the hive and may adversely affect developing brood (egg, larvae, and pupae) and adult bees. Tier II feeding studies are conditional on the outcome of the screening-level assessment where acute and/or chronic risk levels of concern have been exceeded for terrestrial invertebrates based on Tier I studies of individual bees. Feeding studies utilize free foraging bee colonies that are "dosed" with specific quantities of test material and represent a means of ensuring exposure to the test material through spiked pollen and/or sugar solutions fed to the colony while still allowing the bees to forage freely. Since bee colonies are not confined to enclosures, colonies can be exposed for longer duration periods without subjecting the bees to stress that typically results from Tier II tunnel studies. Available toxicity studies of individual bees (Tier 1) conducted to support screening-level assessments do not address possible effects and/or exposure to pesticide residues at the colony-level. It is therefore important to determine whether bee colonies may be negatively affected where bees are free foraging and have the option to collect/consume alternative forage items beyond the spiked food. Since multiple dose levels can be more readily tested, feeding studies can help to define dose-response relationships at the whole colony level. The Office of Pesticide Programs has made available a guidance regarding ecological testing for invertebrates with the honeybee. The guidance describes the tiered testing process and can be found at: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance . Additional information on honeybee colony studies under semi-field conditions can be found in the OECD Guidance 75 http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono%28 .
Practical Utility of the Data
How will the data be used? Tier II colony feeding data will be used to assess potential risk to non-target organisms including listed and non-listed terrestrial social invertebrate species. The colony feeding study is designed to represent potential field-level exposure and account for hive dynamics

using longer duration exposure periods than are possible in Tier II tunnel studies. This study will be used to determine whether potential adverse effects to insect pollinators at the whole colony level when bees are able to forage naturally beyond the spiked food. Results from the feeding study will help to refine the screening-level risk assessment for beneficial terrestrial invertebrates that were based on Tier I studies on individual bees. Since feeding studies can help to define a dose-response relationship at the colony level, the studies can provide a means of determining exposure thresholds below which the likelihood of adverse effects on colonies may be low.

How could the data impact the Agency's future decision-making?

The Tier II colony-level data will be used to refine screening-level risk estimates derived using Tier I laboratory-based data on individual bees. The Tier II data will help to inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect federally listed threatened or endangered species or their designated critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in significant use restrictions.

Field Testing for Pollinators **OCSPP Guideline 850.3040**
Rationale for Requiring the Data
Tier III studies are conditional on the outcome of the screening-level assessment (Tier 1) where acute and/or chronic risk levels of concern have been exceeded for terrestrial invertebrates and where Tier II studies either under semi-field tunnel conditions and/or feeding studies have indicated potential adverse effects at the colony level. Available toxicity studies from lower-tier studies do not address possible effects and/or exposure to pesticide residues at the colony-level under actual pesticide use conditions and where specific uncertainties regarding the likelihood of exposure and/or effects remain. Full-field studies also provide an opportunity to measure residues in pollen and nectar as well as various matrices (beebread, honey, wax) within the colony to obtain a more realistic understanding of exposure. The Office of Pesticide Programs has made available a guidance regarding ecological testing for terrestrial invertebrates using the honeybee as a surrogate test species. The guidance discusses Tier I laboratory-based acute oral toxicity studies of individual adult bees as a critical component of the screening-level risk assessment process for examining potential adverse effects from specific routes of exposure. The guidance can be found at: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance . Additional guidance on the honeybee oral toxicity test design can be found in OECD Test Guideline 213 http://www.oecd-ilibrary.org/environment/test-no-213-honeybees-acute-oral-toxicity-test_9789264070165-en.
Practical Utility of the Data

How will the data be used? Tier III colony-level data will be used to further characterize potential risk to non-target organisms including listed and non-listed terrestrial social invertebrate species and to refine screening-level risk estimates that were based on individual bee responses. The semi-field test is a controlled study that is designed to represent potential field-level exposure under relatively controlled conditions and account for hive dynamics, which are not achievable from lower-tier pollinator studies. This study will be used to determine whether adverse effects to insect pollinators at the whole colony level, may result for the use of pesticides and will help to refine the screening-level risk estimates for beneficial terrestrial invertebrates. This study will also be used to determine whether more refined (Tier 3) studies are needed to characterize risk. **How could the data impact the Agency's future decision-making?** The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect federally listed threatened or endangered species or their designated critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in significant use restrictions.

Study Title: Field Trial of Residues in Pollen and Nectar **Non-guideline Study**
Rationale for Requiring the Data
Terrestrial invertebrates are likely to be impacted if exposed to pesticides residues in various use settings. Pesticide residues may be transferred to pollen and/or nectar of treated plants and subsequently brought back to hive all life stages may be exposed. For some pesticides, the quantification of pollinator-relevant residues in treated flowering plants is needed, since pollinators will be exposed to residues from either current or prior season applications (due to the potential for residues to accumulate in plants and trees). Residues in edible/transportable-to-hive parts of treated trees and plants, including (where appropriate), but not limited to, guttation water, sap/resins, whole plant tissue (*e.g.,* leaves, stems), as well as blooming, pollen-shedding, and nectar producing parts (*i.e.*, flowers and, if present, extra-floral nectaries) of plants may inform the potential for risk. Studies should be designed to provide residue data for crops and application methods of concern. The Office of Pesticide Programs has made available a guidance regarding ecological testing for bees using the honeybee as a surrogate. This can be found at: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance. Since residue studies are intended to provide exposure data in multiple matrices and under specific application conditions, EPA requests that the protocol is submitted for review and approval by EPA prior to initiation of the study.
Practical Utility of the Data

How will the data be used?
Measured residue data will be used to refine conservative estimates of pesticide exposure and reduce uncertainties associated with the Tier I exposure assessment by providing direct measurements of pesticide concentrations resulting from actual use settings. Measured residues may provide a more realistic understanding of exposure through contact or ingestion with which to calculate risk quotients for individual bees as well as to characterize exposure to the colony. If measured residue data are not available, risk estimates for terrestrial insects will be based on model generated or default values used to support the screening-level assessment.

How could the data impact the Agency's future decision-making?
The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect federally listed threatened or endangered species or their designated critical habitat. Without these data, EPA will have to rely on conservative estimates of exposure which may limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in use restrictions.

References

FAO 2000. Appendix 2. Parameters of pesticides that influence processes in the soil. In FAO Information Division Editorial Group (Ed.), Pesticide Disposal Series 8. Assessing Soil Contamination. A Reference Manual. Rome: Food & Agriculture Organization of the United Nations (FAO). http://www.fao.org/docrep/003/x2570e/x2570e00.htm

Duah, F.K, Fisher, J.M., Halder, C.A., Hall, L.R., Hall, T.A., Kelley, I., Tolliver, M.K. and Van Goethem, D. L., 2001. An Overview of the Available Data on 1,2,4-Triazole [Cas No. 288-88-0], a degradate of the Azole Class of Fungicides, and its Relevance to the Risk Profile of Tebuconazole (FOLICUR™). Bayer Corporation. February 27, 2001.

USEPA. 2006 a. 1,2,4-Triazole, Triazole Alanine, Triazole Acetic Acid: Drinking Water Assessment in Support of Reregistration and Registration Actions for Triazole-derivative Fungicide Compounds. D320682. Office of Pesticide Programs Environmental Fate and Effects Division, Environmental Risk Branch 1. February 28, 2006.

USEPA. 2006 b. 1,2,4-Triazole, Triazole Alanine, Triazole Acetic Acid: Human Health Aggregate Risk Assessment in Support of Reregistration and Registration Actions for Triazole-derivative Fungicide Compounds. DP Number 322215. Office of Pesticide Programs Health Effects Division and Environmental Fate and Effects Division. February 7, 2006.

USEPA. 2012 a. Drinking Water Exposure Concentrations for Proposed New Myclobutanil Uses on Grass Grown for Seed, Grass Pastures, Rangeland, and Sod Farms. D403754. Office of Pesticide Programs Environmental Fate and Effects Division, Environmental Risk Branch 3. November 20, 2012.

USEPA. 2012 b. Development and Use of Percent Cropped Area and Percent Turf Area Adjustment Factors in Drinking Water Exposure Assessments: 2012 Update. Office of Pesticide Programs Environmental Fate and Effects Division. May 16, 2012.

USEPA. 2012 c. NAFTA Guidance for Evaluating and Calculating Degradation Kinetics in Environmental Media. December 17, 2012. U.S. Environmental Protection Agency, Office of Pesticide Programs, Environmental Fate and Effects Division. Arlington, VA.

USEPA. 2012 d. Standard Operating Procedure for Using the NAFTA Guidance to Calculate Representative Half-life Values and Characterizing Pesticide Degradation. November 30, 2012. U.S. Environmental Protection Agency, Office of Pesticide Programs, Environmental Fate and Effects Division. Arlington, VA.

USEPA 2014 a. Guidance for Assessing Pesticide Risks to Bees. Office of Pesticide Programs. June 23, 2014.
http://www.epa.gov/pesticides/science/efed/policy_guidance/team_authors/terrestrial_biology_tech_team/GuidanceAssessingPesticideRisk2Bees.pdf

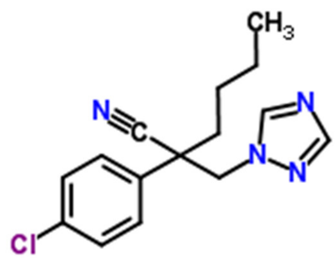
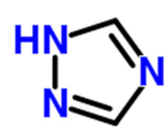
USEPA 2014 b. Myclobutanil Label Use Information System (LUIS) Report. Biological and Economic Analysis Division.

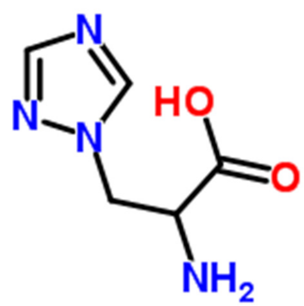
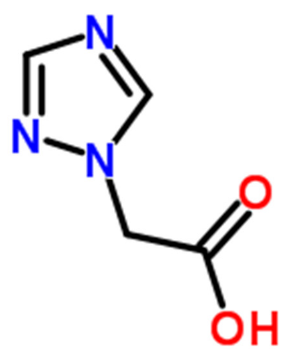
USEPA 2014 c. Myclobutanil Summary Level Usage Analysis (SLUA). Biological and Economic Analysis Division.

Vogel, J.R., M.S. Majewski, and P.D. Capel., 2008. Pesticides in Rain in Four Agricultural Watersheds in the United States. J. Env. Qual. 37:1101-1115.

Appendix A. Myclobutanil Transformation Products

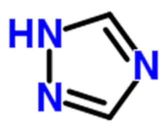
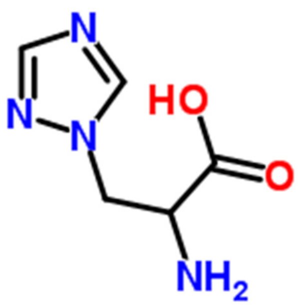
Table A1. Myclobutanil, its Major Transformation Products, and 1,2,4-Triazole Conjugates of Toxicological Concern.

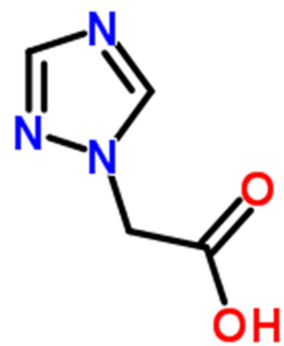
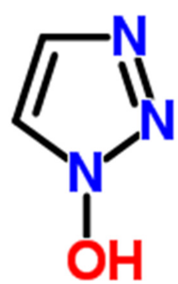
Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum Formation (% Applied) and Day Observed During Study	Final Formation* (% Applied) And Study Length
PARENT						
Myclobutanil	**IUPAC Name:** 2-(4-chlorophenyl)-2-(1H-1,2,4-triazol-1-ylmethyl)hexanenitrile **CAS Number:** 88671-89-0 **Molecular Weight:** 288.775299 g/mol **Chemical Formula:** $C_{15}H_{17}ClN_4$ **SMILES:** CCCCC(CN1C=NC=N1)(C#N)C2=CC=C(C=C2)Cl		**Parent structure shown for reference**			
MAJOR TRANSFORMATION PRODUCTS						
1,2,4-Triazole	**IUPAC Name:** 4H-1,2,4-triazole **Molecular Weight:** 69.0653 g/mol **Chemical Formula:** $C_2H_3N_3$ **SMILES:** C1=NN=CN1		Aqueous photolysis	164560 40319801	**49% (30)**	
			Aerobic soil metabolism	141680 164561	**18% (150, 180)**	13% (367)
			Terrestrial field Dissipation	00164563 00164987	0-3” 22.8% (80) 3-6” 2.9% (363) 6-12” 2.1% (363)	0-3” 3.3% (363) 3-6” 2.9% (363) 6-12” 2.1% (363)
					0-3” 14.4% (47, 160) 3-6” 58.6% (421)	0-3” 6.3% (639) 3-6” not detected (639)

Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum Formation (% Applied) and Day Observed During Study	Final Formation* (% Applied) And Study Length
					6-12” 4.2% (47)	6-12” 5.4% (639)
1,2,4-TRIAZOLE CONJUGATES OF TOXICOLOGICAL CONCERN						
1,2,4-Triazole Alanine	**IUPAC Name:** 2-amino-3-(1H-1,2,4-triazol-1-yl)propanoic acid **Chemical Formula:** $C_5H_8N_4O_2$ **Molecular Weight:** 156.143 **SMILES:** NC(CN1C=NC=N1)C(O)=O		**1,2,4-Triazole Conjugates Not Identified or Not Detected in Available Fate Studies**			
1,2,4-Triazole Acetic Acid	**IUPAC Name:** 2-(1H-1,2,4-triazol-1-yl)acetic acid **Chemical Formula:** $C_4H_5N_3O_2$ **Molecular Weight:** 127.038 **SMILES:** c1ncn(n1)CC(=O)O					

*Maximum % of applied reported at study termination; amounts may have continued to increase with time
Bold indicates maximum % formation percentage of degradate

Table A2. 1,2,4-Triazole, its Major Transformation Products, and its Conjugates of Toxicological Concern.

Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum Formation (% Applied) and Day Observed During Study	Final Formation* (% Applied) And Study Length
PARENT						
1,2,4-Triazole	**IUPAC Name:** 4H-1,2,4-Triazole **Molecular Weight:** 69.0653 g/mol **Chemical Formula:** $C_2H_3N_3$ **SMILES:** C1=NN=CN1		**Parent Structure Shown for Reference**			
1,2,4-TRIAZOLE CONJUGATES OF TOXICOLOGICAL CONCERN						
1,2,4-Triazole Alanine	**IUPAC Name:** 2-amino-3-(1H-1,2,4-triazol-1-yl)propanoic acid **Chemical Formula:** $C_5H_8N_4O_2$ **Molecular Weight:** 156.143 **SMILES:** NC(CN1C=NC=N1)C(O)=O		anaerobic soil metabolism	45930701	**3.4% (7 d post-flood, total system)**	1.4% (122 d post-flood, total system)
1,2,4-Triazole Acetic Acid	**IUPAC Name:** 2-(1H-1,2,4-triazol-1-yl)acetic acid		aerobic soil metabolism	45297203	7.8% (98 d)	3.2% (293 d)

Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum Formation (% Applied) and Day Observed During Study	Final Formation* (% Applied) And Study Length
	Chemical Formula: $C_4H_5N_3O_2$ **Molecular Weight:** 127.038 **SMILES:** c1ncn(n1)CC(=O)O				**18.0% (98 d)**	**11.7% (293 d)**
				45284038	< 0.1% (12 d)	< 0.1% (180 d)
					0.2% (180 d)	
					0.2% (28 d)	
					0.2% (180 d)	
				45284032	6.93% (14 d)	Not Detected (120 d)
					1.67 % (14 d)	Not Detected (120 d)
					0.27% (30 d)	Not Detected (120 d)
			anaerobic soil metabolism	45930701	**50.3% (122 d post-flood, total system)**	
MAJOR NON-CONJUGATE TRANSFORMATION PRODUCTS						
Hydroxytriazole	**IUPAC Name:** 1H-1,2,3-triazol-1-ol **Molecular Weight:** 85.065 **Chemical Formula:** $C_2H_3N_3O$ **SMILES:** On1nncc1		aerobic soil metabolism	45284038	3.1% (61 d)	0.2% (180 d)
					< 0.1 % (180 d)	
					30.8% (12 d)	0.6% (180 d)
					0.9% (60 d)	0.7% (180 d)
					21.5% (12 d)	
				45284032	1.03% (61 d)	Not Detected (120 d)
					Not Detected	
					2.61% (14 d)	Not Detected (120 d)

*Maximum % of applied reported at study termination; amounts may have continued to increase with time
Bold indicates maximum % formation percentage of degradate

Appendix B. SIP analysis inputs and results

Table B1. Inputs

Parameter	Value
Chemical name	Myclobutanil
Solubility (in water at 25°C; mg/L)	142
Mammalian LD_{50} (mg/kg-bw)	1360
Mammalian test species	other
Body weight (g) of "other" mammalian species	20
Mammalian NOAEL (mg/kg-bw)	16
Mammalian test species	laboratory rat
Body weight (g) of "other" mammalian species	
Avian LD_{50} (mg/kg-bw)	498
Avian test species	northern bobwhite quail
Body weight (g) of "other" avian species	
Mineau scaling factor	1.15
Mallard NOAEC (mg/kg-diet)	1250
Bobwhite quail NOAEC (mg/kg-diet)	256
NOAEC (mg/kg-diet) for other bird species	
Body weight (g) of other avian species	
NOAEC (mg/kg-diet) for 2nd other bird species	
Body weight (g) of 2nd other avian species	

Enter body weight of 'other' mammalian species for LD50.

Table B2. Mammalian Results

Parameter	Acute	Chronic
Upper bound exposure (mg/kg-bw)	24.4240	24.4240
Adjusted toxicity value (mg/kg-bw)	511.4420	12.3066
Ratio of exposure to toxicity	0.0478	1.9846
Conclusion*	**Drinking water exposure alone is NOT a potential concern for mammals**	**Exposure through drinking water alone is a potential concern for mammals**

Table B3. Avian Results

Parameter	Acute	Chronic
Upper bound exposure (mg/kg-bw)	115.0200	115.0200
Adjusted toxicity value (mg/kg-bw)	358.7739	27.2124
Ratio of exposure to acute toxicity	0.3206	4.2268
Conclusion*	**Exposure through drinking water alone is a potential concern for birds**	**Exposure through drinking water alone is a potential concern for birds**

*Conclusion is for drinking water exposure alone. This does not combine all routes of exposure. Therefore, when aggregated with other routes (*i.e.*, diet, inhalation, dermal), pesticide exposure through drinking water may contribute to a total exposure that has potential for effects to non-target animals.

Appendix C. STIR analysis results

Welcome to the EFED
Screening Tool for Inhalation Risk

This tool is designed to provide the risk assessor with a rapid method for determining the potential significance of the inhalation exposure route to birds and mammals in a risk assessment.

Input

Application and Chemical Information		
Enter Chemical Name	Myclobutanil	
Enter Chemical Use	Fungicide	
Is the Application a Spray? (enter y or n)	y	
If Spray What Type (enter ground or air)	ground	
Enter Chemical Molecular Weight (g/mole)	288.78	
Enter Chemical Vapor Pressure (mmHg)	9.75E-06	
Enter Application Rate (lb a.i./acre)	1.4	
Toxicity Properties		
Bird		
Enter Lowest Bird Oral LD_{50} (mg/kg bw)	498	
Enter Mineau Scaling Factor	1.15	
Enter Tested Bird Weight (kg)	0.178	
Mammal		
Enter Lowest Rat Oral LD_{50} (mg/kg bw)	1360	
Enter Lowest Rat Inhalation LC_{50} (mg/L)	2.07	
Duration of Rat Inhalation Study (hrs)	4	
Enter Rat Weight (kg)	0.35	

Output

Results Avian (0.020 kg)		
Maximum Vapor Concentration in Air at Saturation (mg/m^3)	1.52E-01	
Maximum 1-hour Vapor Inhalation Dose (mg/kg)	1.90E-02	
Adjusted Inhalation LD_{50}	4.23E+00	
Ratio of Vapor Dose to Adjusted Inhalation LD_{50}	4.51E-03	**Exposure not Likely Significant**
Maximum Post-treatment Spray Inhalation Dose (mg/kg)	1.48E-01	
Ratio of Droplet Inhalation Dose to Adjusted Inhalation LD_{50}	3.50E-02	**Exposure not Likely Significant**
Results Mammalian (0.015 kg)		
Maximum Vapor Concentration in Air at Saturation (mg/m^3)	1.52E-01	

Maximum 1-hour Vapor Inhalation Dose (mg/kg)	2.39E-02	
Adjusted Inhalation LD_{50}	1.23E+02	
Ratio of Vapor Dose to Adjusted Inhalation LD_{50}	1.94E-04	**Exposure not Likely Significant**
Maximum Post-treatment Spray Inhalation Dose (mg/kg)	1.86E-01	
Ratio of Droplet Inhalation Dose to Adjusted Inhalation LD_{50}	1.51E-03	**Exposure not Likely Significant**

Appendix D. Toxicity comparison for myclobutanil and degradates

Table D1. Additional Toxicity Endpoints for Myclobutanil Degradates (1,2,4-triazole, triazole alanine and triazole acetic acid)[1]

Taxonomic Group	Study type	Surrogate Species	Toxicity	MRID (classification)	Comments
1,2,4-triazole (aquatic toxicity)					
Freshwater fish	Acute	Rainbow trout *(Salma gairdneri)*	96-hr LC_{50}= 760 mg a.i./L	00133380/45284017	Under Review
	Chronic (28 day growth toxicity test)	Rainbow trout (*Oncorhynchus mykiss*)	LC_{50}: > 100 mg/L NOAEC (growth) ≥ 100 mg/L NOAEC (sublethal effects) = 3.2 mg/L LOAEC (sublethal effects) = 10.0 mg/L Observed sublethal effects included multiple fish being inactive or displaying abnormally low activity, labored respiration, and lying inactive on the bottom of the aquarium in the three highest concentrations tested between days 23 and 28.	45880405 (Supplemental)	Supplemental due to non-guideline study
	Acute	Rainbow Trout (*Salmo gairdneri*)	96 hr-LC_{50} = 498 mg ai/L NOAEC = 378 mg ai/L (mortality)	48474301 (Acceptable)	None

Taxonomic Group	Study type	Surrogate Species	Toxicity	MRID (classification)	Comments
Freshwater Invertebrates	Acute	Water flea (*Daphnia magna*)	LC_{50} = 900 (730 to 2200, 95% C.I.) mg/L.	00133381	Under Review
	Acute	Water flea (*Daphnia magna)*	48-hr EC_{50} > 98.1 mg ai/L NOAEC = 98.1 mg ai/L (based on mobility, highest concentration tested)	48453206 (Acceptable)	None
Aquatic Plants - Non vascular	Acute	Freshwater Algae (*Pseudokirchneriella subcapitata,* formerly *Selenastrum capricornutum*)	96-hr endpoints: Biomass (most sensitive): EC_{50} = 14 mg ai/L NOAEC = 3.1 mg ai/L Cell Density: EC_{50} = 18 mg ai/L NOAEC = 6.8 mg ai/L Growth Rate: EC_{50} > 31 mg ai/L NOAEC = 6.8 mg ai/L	45880401 (Acceptable)	None
	Acute	Green algae (*Scenedesmus subspicatus*)	EC_{50} = 6.3 (5.5 to 7.1, 95% C.I.) mg/L	00133382	Under Review
1,2,4-triazole (terrestrial toxicity)					
Birds	Acute	Coturnix quail	LD_{50} >316 mg /kg bw	45284015	Under Review
	Acute	Bobwhite quail (*Colinus virginianus*)	LD_{50} = 770 mg /kg bw	49380701	Under Review
Mammals	Acute	Laboratory mouse *(Mus musculus)*	LD_{50} = 3650 mg/kg	45284001	Review not available[2]
	Acute	Laboratory Rat (M)	LD_{50} = 1375 mg/kg	45284008	Reviews not available[2]

Taxonomic Group	Study type	Surrogate Species	Toxicity	MRID (classification)	Comments
		(Rattus norvegicus)	LD_{50} = 1648-3080 mg/kg	45284004, 45284001	
	Reproduction and fertility effects 0, 250, 500, 3000 ppm M: 15, 31, 189 mkd F: 18, 36, 218 mkd	Laboratory rat *(Rattus norvegicus)*	Parental NOAEC/NOAEL <250 ppm/15 mg/kg/day Parental LOAEC/LOAEL= 250 ppm/15 mg/kg/day based on decrease in bodyweight, bodyweight gain and spleen weight. Offspring NOAEC/NOAEL= <250 ppm/19 mg/kg/day Offspring LOAEC/LOAEL= 250 ppm/19 mg/kg/day based on decrease in bodyweight, bodyweight gain, brain and spleen weights Repro NOAEC/NOAEL= 250 ppm/15 mg/kg/day Repro LOAEC/LOAEL= 500 ppm/31 mg/kg/day based on abnormal sperm and ↓# of CL in F_1 females At 3000 ppm/218 mg/kg/day, reproductive failure (no viable offspring), ↑CL in F_0 parental females	46467304 (Acceptable)	None

Taxonomic Group	Study type	Surrogate Species	Toxicity	MRID (classification)	Comments
	Developmental Toxicity in Rabbits 0,5,15,30,45 mg/kg/day	New Zealand white rabbit	Parental/developmental NOAEL= 30 mg/kg/day Parental/developmental LOAEL= 45 mg/kg/day based on mortality and clinical signs (decreased motor activity, head tilt, lacrimation, drooping eyelids, diarrhea and salivation) for parental effects and decreased fetal weight and urinary tract malformations for developmental effects Mortality (6/25 rabbits) in 45 mg/kg/day group	46492903 (Acceptable)	None
Terrestrial Invertebrates	Acute and reproductive (28 days)	Collembolan (springtails) Species (*Folsomia candida)* soil arthropods	LC_{50}>10 mg/kg NOAEC (mortality) ≥ 10mg/kg NOAEC (reproduction) = 1.8 mg/kg	45880404 (Supplemental)	Non-guideline study
	Growth and reproductive (8 weeks, adult 28 day exposure, additional 4 week offspring exposure)	Earthworms (*Eisenia fetida)*	LC_{50}> 70.81 ug/kg NOAEC ≥ 70.81 ug/kg (highest concentration tested) No significant treatment effects for mortality, behavior, body weights, reproduction or food consumption	45880402 (Supplemental)	Non-guideline study
Triazole alanine (aquatic toxicity)					

Taxonomic Group	Study type	Surrogate Species	Toxicity	MRID (classification)	Comments
No submitted data identified					
Triazole alanine (terrestrial toxicity)					
Mammals	90-day oral toxicity in rodents – rat 0, 1250, 5000, 20000 ppm M: 0, 90, 370, 1510 mg/kg/day F: 0,160, 400, 1680 mg/kg/day	Laboratory rat *(Rattus norvegicus)*	NOAEL = 90/160 mg/kg/day (M/F) LOAEL = 370/400 mg/kg/day (M/F) based on decreased leukocyte counts and decreased triglycerides in females At 1510/1680 mg/kg/day (M/F) decreased body weight (M), body weight gain (M), leukocytes (M/F) and triglycerides (M/F)	00164107 (Acceptable)	None
	Reproduction and fertility effects 0, 200, 2000, 10000 ppm M: (F0/F1) 0, 50/47, 213/192, 1098/929 mg/kg/day F: 0, 51/49, 223/199, 1109/988 mg/kg/day	Laboratory rat *(Rattus norvegicus)*	Parental NOAEC/NOAEL= 10000 ppm/929 mg/kg/day Parental LOAEC/LOAEL: >10000 ppm/929mg/kg/day Offspring NOAEC/NOAEL <250 ppm/19 mg/kg/day Offspring LOAEC/LOAEL=2000ppm/192 mg/kg/day based on reduced mean litter weights in both generations Repro LOAEC/LOAEL>10000	00164112 (Acceptable)	None

Taxonomic Group	Study type	Surrogate Species	Toxicity	MRID (classification)	Comments
			ppm/929mg/kg/day		
Triazole acetic acid (aquatic toxicity)					
Freshwater Fish	Acute	Rainbow trout (*Oncorhynchus mykiss*)	96 hr-LC_{50} >101 mg ai/L NOAEC = 101 mg ai/L (mortality/sub-lethal effects)	48453209 (Acceptable)	None
Freshwater Invertebrates	Acute	Water flea (*Daphnia magna)*	48-hr EC_{50} > 108 mg ai/L NOAEC = 108 mg ai/L (based on mobility, highest concentration tested)	48453208 (Acceptable)	None
Triazole acetic acid (terrestrial toxicity)					
Mammals	Acute	Laboratory rat *(Rattus norvegicus)*	LD_{50} > 5000 mg/kg	45596802	Review not available[2]
	14 day oral toxicity in rodents 0, 100, 1000, 8000 ppm M: 0, 10.6, 102.8, 788.3 mg/kg/day F: 0, 10.1, 97.2, 703.5 mg/kg/day	Laboratory rat *(Rattus norvegicus)*	NOAEL = 788.3/703.5 mg/kg/day (M/F) LOAEL >788.3/>703.5 mg/kg/day (M/F)	45596801	None

1 Many endpoints derived from summary document USEPA 2006 b. 1,2,4-Triazole, Triazole Alanine, Triazole Acetic Acid: Human Health Aggregate Risk Assessment in Support of Reregistration and Registration Actions for Triazole-derivative Fungicide Compounds.

2 Values taken from triazole aggregate study referenced above, where it was noted that some values were from submitted summary data and full study reports were not available.

Table D2. Summary table of comparable toxicity data for myclobutanil and major degradate 1,2,4-triazole and its conjugates triazole alanine and triazole acetic acid[1]

Taxonomic group	Study type	Myclobutanil	1,2,4-triazole	Triazole Alanine	Triazole acetic acid
Freshwater fish	Acute 96-hr LC_{50}	2.4 mg/L (Bluegill sunfish)	498 mg/L (rainbow trout)		>101 mg/L
	Chronic	NOAEC =0.98 mg/L (fathead minnow)	3.2 mg/L (rainbow trout)		
Estuarine/marine fish (sheepshead minnow)	Acute 96-hr LC_{50}	4.7 mg/L			
	Chronic	--			
Freshwater Invertebrates (water flea)	Acute 48-hr EC_{50}	11 mg/L	> 98.1 mg/L		>108 mg/L
	Chronic	NOAEC = 3.9 mg/L (based on ACR analysis)			
Estuarine/marine invertebrates (mysid shrimp)	Acute 96-hr LC_{50}	0.24 mg/L			
	Chronic	NOAEC = 0.0856 mg/L (LOAEC > 0.0856 mg/L, no effects seen)			
Aquatic Plants (Green algae)	120-hr EC_{50}	0.83 mg/L	6.3 mg/L		
Birds (Bobwhite quail)	Acute LD_{50}	498 mg/kg bw	770 mg/kg bw		
	Chronic	NOAEC = 256 mg/kg diet (LOAEC >256 mg/kg diet, no effects seen)			
Mammals	Acute (mouse LD_{50})	1360 mg/kg bw	3650 mg/kg bw	>5000 mg/kg bw	
	Acute (rat LD_{50})	1600 mg/kg bw	1375 mg/kg bw		
	Chronic (rat NOAEL)	16 mg/kg bw	15 mg/kg bw	703.5 mg/kg bw	19 mg/kg bw

[1] See Tables 7-9 for individual study details.

Table D3. Comparison of ECOSAR outputs for myclobutanil and major degradate 1,2,4-triazole (and its conjugates triazole alanine and triazole acetic acid) and hydroxytriazole

Taxonomic group	Study type[1]	Myclobutanil	Myclobutanil	Myclobutanil	1,2,4-triazole	Triazole Alanine	Triazole Acetic Acid	Hydroxytriazole
		Study Value (mg/L)	ECOSAR Class: Benzyl Nitriles (mg/L)	ECOSAR Class: Triazoles (Non-fused) (mg/L)				
Freshwater fish	96-hr LC_{50}	**2.4**	10.9	33	3574.08	3.97×10^{7}*	3.96×10^{5}	7837.86
	Chronic Value	**NOAEC = 0.98**	1.73	0.116	2.465	5279.28	169.42	4.637
Estuarine/marine fish	96-hr LC_{50}	**4.7**	17.4	96.423	14610.51	2.28×10^{8}*	1.79 x 106*	33075.76
	Chronic Value	**--**	--	0.189	0.350	63.34	11.77	0.524
Freshwater Invertebrates	96-hr LC_{50}	**11**	110	9.9	49.73	24526.29	2234.26	84.61
	Chronic Value	**NOAEC = 3.9 (based on ACR analysis)**	1.059	0.966	22.77	53985.50	1611.60	43.24
Estuarine/marine invertebrates	96-hr LC_{50}	**0.24**	1.086	9.612	1309.41	1.84×10^{7}*	1.55×10^{5}	2934.67
	Chronic Value	**NOAEC = 0.0856 (LOAEC > 0.0856, no effects seen)**	--	14.987	126000	1.15×10^{11}*	4.99×10^{7}*	4.16×10^{5}
Aquatic plants (green algae)	96-hr LC_{50}	**0.83**	2.568	5.762	79.46	1.09×10^{5}*	4806.58	143.48
	Chronic Value	--	1.562	5.074	59.008	68398.53	3395.29	104.85

* = asterisk designates: Chemical may not be soluble enough to measure this predicted effect. If the effect level exceeds the water solubility by 10X, typically no effects at saturation (NES) are reported.

[1] Chronic values not available for some taxonomic groups